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ANALYSIS OF A PREFRONTAL LOBE SYNDROME AND ITS THEORETIC IMPLICATIONS

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THE PREFRONTAL regions of the brain present difficult problems for investigation, which have led to divergent findings and opinions and have caused considerable perplexity to most workers in the field. The behavioral and intellectual changes which may follow lesions in the frontal regions are difficult to isolate and compare. Differences in the severity of the deteriorations, the localization and nature of the lesions, the intellectual assets and the general personality traits of the patients, as well as the variations in the technics employed and the persons employing the technics, have presented unavoidable complications. There is good evidence that unilateral, and even bilateral, removal of the prefrontal region may cause no perceptible defect. The fairly typical clinical syndrome formerly attributed to frontal lobe dysfunction may depend on involvement of other portions of the brain. Studies based on expanding lesions or presenile deteriorations have required reevaluation. Hebb's [1] critical evaluation of frontal lobe studies has shown that uncomplicated removals of tissue are rare and that, at present, reliance must be placed on the studies in which little or no change followed lobectomy rather than on so-called typical cases. However, the absence of behavioral defect following lobectomy does not mean that lesions in the frontal region may not produce dysfunction, but indicates only that patients seem capable of acting normally after the damaged areas are removed, perhaps by utilization of other mechanisms. The studies of the effects of frontal lobotomy are also diffi-

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Dr. Samuel Barkoff, now of New Orleans, brought the patient to my attention and collaborated in the initial studies; Dr. John C. Whitehorn made valuable suggestions in editing the script; Dr. W. Horsley Gantt made the conditioned reflex studies; Dr. Richard Lyman made the electroencephalographic studies; Dr. Alexander Leighton and Mr. Theodore Czarski aided with the sound films, and Miss Cecelia Bisson prepared the pathologic sections and photographs.

1. Hebb, I. O.: Man's Frontal Lobes, Arch. Neurol. & Psychiat. **54**:10 (July) 1945.

cult to resolve. Although a profound change in personality usually occurs, intellectual deficits cannot be found in some patients, though obvious in others. It is likely that the results of the operation vary with the precise localization of the lesions produced. Frontal lobotomies have called attention to the fact established by Stern [2] that disruption of the tracts passing to and from the frontal lobes and the thalamus produces a symptomatology which was once considered diagnostic of lesions of the frontal lobe.

Whether due to changes in the frontal lobe or in adjacent structures, lesions in the area have given rise to behavioral patterns which have common features and qualities. The excellent descriptions of behavioral patterns following lesions of the frontal lobe by Ackerly,[3] Brickner,[4] Nichols and Hunt,[5] Rylander,[6] Goldstein and Katz,[7] Freeman and Watts [8] and others show striking similarities, despite variations in the severity of the impairment. The search after a unifying basic defect has been unsatisfactory. Although similar trends run through the several hypotheses, a theory that clarifies one case meets with objections when applied to another.

The study to be presented here is concerned with a case in which greater limitations followed damage to the frontal lobe than in any case reported in detail. It is believed that the extreme simplification of the patient's behavior and intellectual functioning permits the clarification of basic concepts that contribute to the theory of frontal lobe function in particular and of symbolic processes in general.

The patient first attracted attention because he displayed features considered typical of frontal lobe lesions to an extent that made him appear a caricature of the syndrome. Absence of initiative and apathy were mingled with euphoric disregard of his dismal surroundings. Everything was "fine and dandy." His sparse remarks were flavored

2. Stern, K.: Severe Dementia Associated with Bilateral Symmetrical Degeneration of the Thalamus, Brain **62**:157, 1939. Smyth, G. E., and Stern, K.: Tumors of the Thalamus: Clinico-Pathological Study, ibid. **61**:339, 1938.

3. Ackerly, S.: Instinctive, Emotional and Mental Changes Following Prefrontal Lobe Extirpation, Am. J. Psychiat. **92**:717, 1935.

4. Brickner, R. M.: The Intellectual Functions of the Frontal Lobes, New York, The Macmillan Company, 1936.

5. Nichols, I., and Hunt, J. M.: A Case of Partial Bilateral Frontal Lobectomy: A Psychopathological Study, Am. J. Psychiat. **96**:1063, 1940.

6. Rylander, G.: Personality Changes After Operation on the Frontal Lobes, Acta psychiat. et neurol. (supp. 20), 1939.

7. Goldstein, K.: The Significance of the Frontal Lobes for Mental Performance, J. Neurol. & Psychopath. **17**:27, 1936. Goldstein, K., and Katz, S. E.: Psychopathology of Pick's Disease, Arch. Neurol. & Psychiat. **38**:473 (Sept.) 1937.

8. Freeman, W. J., and Watts, J.: Psychosurgery, Springfield, Ill., Charles C Thomas, Publisher, 1942.

by witzelsucht. Though he was usually polite and diffident, there was also lack of normal restraint when aroused. Intellectual deficits were obvious; speech and behavior was stereotyped; memory was defective, and insight into his impairments was completely lacking. His appetite seemed insatiable at times. Despite the severity of his disabilities, there remained a fairly large range of behavior that seemed adequately intelligent and appropriate. He was far from dilapidated, remaining a distinct personality, albeit a shell of his former self. The behavioral pattern had been simplified to a degree that permitted predictability of response to many situations. Increase in predictability through study offered a check on the validity of the insights attained. His condition had remained static for eight years before the study started, making the presence of a progressive lesion unlikely.

The initial impression that the lesions were localized and static was confirmed after postoperative death. The left prefrontal regions, particularly the frontal pole, were atrophied as a result of an old vascular lesion, which had also involved the anterior limb of the internal capsule and a portion of the caudate nucleus. In addition, a very small, discrete softening involved a portion of the anterior capsule on the right. The brain was otherwise free of vascular involvement. The areas of destruction were not as extensive as those found after frontal lobotomy, even though the intellectual defects were far greater. On the other hand, the intellectual impairment was not as marked as in the case reported by K. Stern,[2] in which little was found other than bilateral degeneration of the dorsomedian thalamic nuclei. This case clearly does not provide crucial evidence concerning the correlation of anatomic localization of lesions with the severity of personality dysfunction. The study is concerned rather with the psychologic analysis of the defect in mentation and its influence on behavior.

The patient was studied for eight months by observation while in various settings and by a wide variety of test situations. At times, almost everything said or done by the patient during the day was recorded. The observations were supplemented by sound motion picture recordings,[9] which permitted repeated review of the patient's productions and served to amplify the written records. The individual tests were regarded as samplings of behavior under controlled conditions, which could be evaluated only after scrutiny of precisely what the procedure tested and of the conditions under which they were carried out. Such care in evaluation seems essential for the avoidance of errors that can arise from emphasis of the results of a single test or group of tests. Comparative material was gathered by the examination

9. Leighton, A. H., and Lidz, T.: The Talking Pictures in Psychiatric Teaching and Research, Am. J. Psychiat. **98**:740, 1942.

and testing of patients with other organic syndromes (some of which have been published elsewhere[10] and some of which remain to be published) to help in differentiating specific disabilities from those common to various deficit states.

The mass of material accumulated during the study has been carefully condensed for presentation. Many procedures were necessary to find direction; some, to eliminate alternative considerations; some were found too vague and became useful only when broken into components; some tested beyond his capacities, and many were simply found redundant, testing different aspects of the same thing. However, an effort is made to offer sufficient sampling of typical behavior and significant procedures to permit critical evaluation of the approach, the analysis of the material and the conclusions attained. It is believed that certain fundamental principles evolved give order and meaning to a behavioral pattern that was extremely perplexing when first observed, and eliminate the discrepancies between good and poor performance which have been puzzling in the study of organic deficit states.

ANALYSIS OF CASE MATERIAL

HISTORY

F., a married man aged 50, had been hospitalized in a state institution for seven years with the diagnosis of "unclassified psychosis" when the present study was undertaken. It was possible to reconstruct the history of his illness and gain a picture of his earlier life by reviewing the careful records which had been retained by a competent neuropsychiatrist, and through interviews with his wife and fomer intimate associates.

One morning in 1917, when he was 28 years old, F. awoke unable to speak and became badly upset. Speech returned rapidly, but for a few days he complained of "weakness, trembling and loss of confidence." His difficulties were attributed to a "nervous breakdown," due to overwork. After several weeks of rest, F. returned to his work as a private secretary, fully recovered. His health remained excellent during the ensuing twelve years, except that on one occasion, when he was about 32, things went blank for a moment and he was unable to find the word he wished to say. His work record was excellent, and he was advanced to a position of considerable responsibility as private secretary to the attorney general of the large railroad for which he worked. At the age of 40, F. suffered another "breakdown" similar to the first. It was again attributed to overwork. He may not have had transient speechlessness, but he complained of inability to concentrate and of weakness and "trembling." A few weeks of vacation again enabled him to return to work. No diminution of his competence

10. Lidz, T.; Gay, J. R., and Tietze, C.: Intelligence in Cerebral Deficit States and Schizophrenia Measured by Kohs Block Test, Arch. Neurol. & Psychiat. **48**:568 (Oct.) 1942. Lidz, T.: The Amnestic Syndrome, ibid. **47**:588 (April) 1942. Lidz, T., and Kahn, R. L.: Toxicity of Quinacrine (Atabrine) for the Central Nervous System: III. An Experimental Study on Human Subjects, ibid. **56**:284 (Sept.) 1946.

was noted. Then, just a year later, when he was 41, F. found himself unable to get his work done and complained of extreme fatigue and weakness. After several weeks he was referred to a neuropsychiatrist, who found F. depressed and apprehensive, complaining that the responsibilities of his position and the long hours of work had worn him down. He still complained of weakness, difficulty in concentration and a feeling that his body was trembling all over. No neurologic abnormalities were found. A verbatim record of examination of the mental status was made. It shows clearly that at this time F.'s intelligence was superior, his grasp of the situation excellent and his memory intact. After several months of regulated activity he was permitted to return to work, admonished not to let overconscientiousness lead him to overwork.

Two years later, when 43 years old, F. was again referred to the same neuropsychiatrist. The alteration in personality was striking, shown clearly by comparison of the verbatim records. No evidence of a sudden change in behavior could be elicited. However, it is possible that F. had been retained at his work after the previous illness only because of his excellent record. During the year following his return to work, he had on three occasions abruptly stopped speaking, stared straight ahead and begun to stammer. The lapses were only momentary, and he had commented each time that he had been unable to form the word he had wished to say and had felt as if he were going to have a spell. His behavior altered gradually. It became necessary to transfer him to simpler duties. Work was taken lightly and irresponsibly. He frequently absented himself from work and offered stereotyped excuses. It was learned that he would often spend the day in a movie seeing the same picture over and over. He borrowed money and never repaid. At home, interests diminished until he wished to do nothing except play cards. He embarrassed his wife with constant repetition of a few stereotyped remarks and by his forgetfulness. He became restless, indifferent and devoid of insight and initiative. The neuropsychiatrist now noted a coarse tremor of the head and hands and a disturbance of articulation. Behavior and content were essentially the same, as will be described in detail later. There seems to have been little, if any, change in F.'s condition from the time he was hospitalized, at the age of 43, until his death.

Reconstruction of F.'s early life remained faulty, for no close blood relatives were alive. Born in Baltimore, he had completed high school at the age of 17. He had always been considered extremely bright. While working as a clerk, he studied stenography in his spare time and, at 19, gained employment with the railroad, where he advanced rapidly. He was known to his co-workers as a diligent man who avoided the distractions of personal conversation. His alertness and the rapidity of his responses were extraordinary. The attorney for whom he had worked still considered F. to have been the most competent secretary he had ever employed; and stressed F.'s good judgment in handling responsibilities prior to his illness. F. married at the age of 23 and remained a devoted husband and father until hospitalized. His habits, aside from excessive smoking, were exemplary. In contrast to his retiring behavior at work, his friends considered him a witty and entertaining companion. He played the piano by ear and was able to play a tune after hearing it once. He enjoyed clowning at parties and was sought after as an entertainer, for he would sing, play the piano and imitate famous personages. His major diversions had always been card playing and the piano.

The family history could not be learned in any detail, but it is known that his father and one or two brothers had died of cerebral vascular accidents at relatively early ages.

F.'s physical condition remained essentially unchanged during the seven years preceding his death. A constant tremor of the head, which was usually held slightly tilted, and a fairly constant tremor of the arms were always noted. Deep reflexes were hyperactive throughout, but no abnormal reflexes were ever elicited. There was a peculiar disturbance of gait—a slovenliness of leg movement that was difficult to define. The vacuous facial expression with lax musculature would change instantly into a broad grin on appropriate stimulation. No physical signs which might have been helpful for localization of a lesion in the frontal regions could be found. Aphasic and apraxic difficulties were never present. On his admission to the state hospital, a slight elevation was found in the protein content of the spinal fluid, but examinations in later years showed a normal level. Several years after his admission it was noted that he was habitually incontinent of urine, but no reason for the incontinence except inattention could be found.

In January 1939 the present study was started. The physical findings remained as already described. Electroencephalographic studies indicated a lesion of the left frontal cortex. After three months of study at Springfield State Hospital, F. was transferred to the Henry Phipps Psychiatric Clinic, where daily behavior could be followed more intimately. After five more months of study, an exploratory craniotomy was performed, the left frontal cortex was found to be shrunken and the left prefrontal regions were excised, in the hope that removal of the damaged regions would improve his condition.[11] Unfortunately, hyperthermia of central origin developed, and, after fourteen days of high fever, F. died. There was no appreciable change in his mental condition following operation. He remained euphoric and oblivious to discomfort.

GENERAL BEHAVIOR

F. had led a vegetative existence in the state hospital for more than six years. The description of his behavior and the content of his talk recorded on his admission, and on subsequent occasions while there, were essentially the same as during the period of study. F. ran away on several occasions during the first two years of hospitalization, and then even this show of initiative disappeared. Although at liberty to wander around the grounds, he usually sat about doing nothing. Efforts to interest him in work or recreational activities soon were given up, and he became one of the idlest in a cottage for idle men. Activities were limited to joining in a game of cards when invited and to smoking cigarets. When his own supply of cigarets was exhausted, he asked other patients for their butts. Occasionally he sang old songs, but usually he sat quietly until meals were ready or it was time to go to bed. He was habitually incontinent of urine but took care of his bowel habits. Visits from his wife were awaited eagerly, but he did not seem disappointed if she failed to appear on visiting days. There was no fretting over his confinement, although, when asked, he insisted that he was fully recovered and could return to work.

During the five months in the Henry Phipps Psychiatric Clinic it was possible to observe his behavior closely, and often to record virtually everything he did or

11. Nielson, J. M., and Raney, R. B.: Recovery from Aphasia, Arch. Neurol. & Psychiat. **42**:189 (Aug.) 1939. Stookey, B.; Scarff, J. E., and Teitelbaum, M. H.: Frontal Lobectomy in Treatment of Tumors in the Anterior Cranial Fossa, ibid. **42**:969 (Nov.) 1939.

said during the day. An interesting change in behavior occurred. With nurses and attendants constantly guiding him into planned activities, there was a cessation of idleness. Within a week, by following the example of fellow patients, he recovered manners long neglected in the state hospital setting.

On casual observation, little that was unusual might be noted, aside from the tremor of the head, for F. volunteered little and he retained well organized social presence. He was a pleasant patient, almost always affable, walking about quietly and listening to the conversations of others without intrusion, except to chime in with meaningless little remarks, which were often a repetition of the last phrase spoken. If asked how he was feeling, he would always reply, "Fine and dandy." The trace of a grin, habitually present, broadened into a smile when he greeted any one. If others laughed at him, he was pleased, apparently feeling that they were laughing with him. Occasionally he became boisterous, particularly when he sang with or against the radio, or if tormented by a manic patient in the ward. There were rare outbursts of temper, always instigated by the manic patient, when F. would start cursing. F. would continue cursing until reprimanded, when he would pause to apologize, "Sorry, I won't do it again," only to renew the barrage immediately unless he was diverted.

Despite the general leveling of affect on a euphoric plane, there was responsiveness to situations which was often, though not always, appropriate. When his wife visited, he said little, but grinned from ear to ear. He greeted her affectionately on her arrival and departure. After she left, F. would report, "My wife was here—she's got some figure, and she kissed me goodbye—oh boy!" or, "My wife gave me two packs of cigarets; hot dog!" When his former employer, the attorney, visited him for the first time in six years, F. jumped from his chair, trembling visibly with joy; but the conversation came to a halt within a few minutes, when the attorney had exhausted his questions. F. asked him for cigarets and then, after a few minutes, excused himself to leave with other patients to play pool.

With guidance, F. followed the ward routine, participating to some extent in almost all activities. His table manners soon became adequate to permit his dining with other patients. He joined in occupational activities by weaving the simplest type of basket, murmuring, "Over one, under one", as he worked the reed around the struts. It was noted that he was unable to work without saying the formula. His work was very poor, but it made no difference to him when, as frequently happened, an hour's work had to be ripped. In carpentry shop he sandpapered wood but would keep sandpapering the same spot for an hour unless reminded to shift. As he worked, he sang snatches of old tunes and frequently interrupted his activity to take a drink of water or to go to urinate. During the rest hour he would lie quietly, but, even though taken to the lavatory immediately before, would usually wet the bed. He did not play volley ball but watched idly, and, knowing that nourishment followed exercise, he would rush to the tray on returning to the ward and eat greedily. At supper time he helped arrange the chairs and tables after some one else had started it, without being asked. When the radio played, he would often sing boisterously, not noting the annoyance he caused. In the evenings he enjoyed playing cards, joining the game of Five Hundred even when not asked, oblivious to the reluctance of others to play with him. On occasions he would play passably well for a short time, and would even keep score; but usually he followed poorly, unaware of the bid, and failed to follow suit. At times he would trump his partner's trick and play against him. When no one took in a trick, he would take it whether it was his or not. Although he

seemed able to adhere to the general form of the game, his playing deteriorated rapidly as he became boisterous, singing as he played, or saying, "Sorry," or *"Danke schön,"* each time he threw out a card. Checker playing was of the same order, usually according to the rules; but it was noted that he never planned a move in advance and at times would lapse and move his opponent's men. In contrast to cards and checkers, which he had played before his illness, he was unable to learn Chinese checkers, a simpler game, despite considerable instruction. He was not above appropriating a package of cigarets left lying about. When cigarets were not obtainable, he might smoke stub tobacco rolled in toilet paper, or even the rolled paper alone. He displayed sufficient initiative to request other patients to give him their butts, and then to suggest that they were smoking them too far. When other patients had visitors, he would draw up a chair without having been invited and sit with the group as though he were a member of the family.

Lack of initiative was striking, for his actions were habitual and sterotyped—a small variety of set responses to given situations. Actions which arose from within himself were mainly in response to needs, such as going to the toilet, eating or asking for cigarets, or from well ingrained routine, such as going to bed and dressing. The customary range of talk was highly stereotyped and will be analyzed later. He utilized a few phrases which he knew would draw a smile from his listeners. The poverty of initiative was partially masked by the ease with which he was led. He was open to stimulation from others. The manic patient would take F. in tow and temporarily alter his behavioral pattern. F. sang whenever the other patient sang, often competing for dominance in volume. The manic patient soon learned that he could inevitably create excitement by calling F. names, which produced a barrage of vulgarity in return. And the request, "Come on F.; let's hear you sing," would never fail to bring forth the strains of "Put on Your Old Gray Bonnet" or "Sweet Adeline."

Although F.'s usage of his stereotyped patterns of response was often inappropriate, he showed some discrimination for persons and circumstances. Although he could be vulgar with other patients, he was always courteous to nurses and physicians. He would customarily wink at the nurses to be companionable but was never truly disrespectful. If a physician refused the habitual request for a cigaret, he would mumble a humble, "Sorry," whereas a refusal by the manic patient might start a flow of cursing.

Before proceeding to the more detailed scrutiny of F.'s capacities and incapacities, the following salient characteristics of his behavior are summarized.

1. He retained capacities at an adult level but was unable to learn anything new beyond simple routine. Manner, apologetic reserve and adherence to social amenities covered the profundity of his inadequacies. The ability to continue to some extent to carry out former acquisitions masked his inability to learn simple new procedures.

2. The absence of initiative led to total idleness, but activity could be aroused by stimulation from others.

3. His rather constant euphoria was expressed by his routine phrase "Fine and dandy."

4. He lacked a normal degree of restraint, which was evident when he was provoked.

5. His faulty appreciation of the situation often led to inappropriate behavior.

6. He had total lack of insight into his condition.

7. He displayed the peculiar sort of humor known as witzelsucht, which will be more evident in examples given later.

Without elaborating at this point, it is apparent on consideration that the characteristics designated are interrelated and are not clearly separable.

VERBAL PRODUCTIONS

F.'s talk resembled his general behavior in many ways. Except for highly stereotyped remarks, he depended on external stimulation for initiation and direction. His talk appeared a direct manifestation of his mentation. There was very little evidence of "internal speech" in Vigotsky's sense,[12] but an acceptance of his responses in uncritical fashion would lead to an improper estimation of his abilities.

The most striking feature of F.'s talk was the rapidity of his utterances. Responses were emitted so quickly that they were difficult to understand. Answers were sometimes started before the question had been completed. A single phrase comprised the entire answer and might consist simply of, "I don't know," even though the answer lay within the range of his information. When asked for further comment, F. sometimes added another simple phrase, but usually he would insist, "That's all I know, doctor," or would repeat the same answer over and over without elaboration. There was no pause for consideration, but, rather, an automatic firing off of the first association provoked. A large number of his replies appeared to be meaningless, and at first seemed completely arbitrary.

Some stereotyped replies, however, like his stereotyped behavior, helped maintain a semblance of social contact. Any question pertaining to health, mood or his opinion of something brought forth an automatic, "Fine and dandy," or a rare, but equally abrupt, "Lousy." A motor response to a request was often preceded by, "O.K., Butch." Questions regarding the reasons for his hospitalization produced, "Because of a nervous breakdown in the office," to which he occasionally added, "I shook all over." Responses to customary questions became ingrained and were not varied to meet new circumstances. The response "Springfield State Hospital" had served so long as the answer to the question "Where are you?" that after several months at the Phipps clinic he continued to respond "Springfield State—no, Johns Hopkins Hospital." His customary response to queries concerning what had been done at the last interview was, "You examined me all over," but for months after the electroencephalographic studies he continued to add the phrase, "by putting wires on my head," even though questioning showed that he knew what had actually happened.

Spontaneous remarks were rare. Actually, most spontaneous speech was exclamatory, even when the words were not those customarily used by others for exclamation. Such phrases as, "Put on your old gray bonnet," had somehow acquired an emotional connotation and sounded nonsensical if this was not appreciated. The interpolation of meaningless little phrases into the conversation of others maintained an impression of social participation. Sometimes F. would repeat the last phrase of another's remarks. If a remark had an affirmative connotation, such as, "It's a wonderful day," F. might hasten to chime in, "Yes, indeedy," whereas a negative implication, such as, "It's not a nice day," might elicit, "No, not nice at all." The tendency to confirm positive and negative implications had to be watched closely while testing the patient, for it could, at times, exert a greater influence on the answer than the actual question. Occasionally these participating remarks broadened out slightly, as when two physicians were conversing in his presence and one remarked with surprised intonation, "Why, today is Wednesday!" and F. interpolated, "Yes, today is Wednesday and

12. Vigotsky, L. S.: Thought and Speech, Psychiatry **2**:29, 1939.

tomorrow is Thursday." The longest single remark during the period of study came in response to a simple, "Good morning," when he volunteered in a single emission of breath, "My wife is coming today—if I had a Packard roadster and a bottle of liquor and two packs of cigarets, oh boy!" This remark, too, was really an amplified exclamatory ejaculation. It may be said that F. never carried on any actual conversation.

A question could evoke a definite answer, but, even when dealing with very familiar material, it was always limited to a simple phrase. Lack of elaboration did not mean that no further material was available, and even protestation by the patient, "That's all I know," indicated only that nothing further was available spontaneously. Further direct questions produced proper replies. Each response remained in virtual isolation and did not arouse further associated material. He had to be led into each associational trend by a new question. The following conversation, selected from many recorded as one of his best performances, deals with an extremely familiar topic.

"Q. Tell me everything you know about your wife. F. She's pretty and well built and some good cook at home. Q. Tell me more about her. F. She dances and sings. Q. Is that all you know? [negative implication]. F. That's all I know. Q. How many years did you live with her? F. Twenty-nine years [incorrect]. Q. And that's all you know about her? F. That's all I know. She was only sick once—she suffers from sick headaches. Q. How old is she? F. Forty-six. Q. Where was she born? F. Germany. Q. What's her name? F. Betty—her proper name is Elizabeth F. Q. What does she do? F. Work's at R.'s, on West Baltimore Street. Q. What does she do there? F. Saleswoman. Q. When did she come to Baltimore? F. When 15. Q. Did she come alone? F. No, with her people—father, mother, sister and brother. Q. When did you meet her? F. When I was 22. Q. Were you in love with her? F. Sure I was! Q. How was married life? F. Fine and dandy, every inch of it. Q. Now what have you told me? F. She's pretty and well built and some good cook at home—she dances and sings and suffers from sick headaches. Q. You told me more—what else did you tell me? F. That's all—she's pretty and well built and some good cook at home—she dances and sings—and suffers from sick headaches—she was born in Germany and came to this country at 15 with her father, mother, brother and sister. Q. What else can you tell me? F. That's all I can think of, doctor. Q. Are you sure? F. That's all I can think of, doctor."

This was one of his optimal performances. It is seen that there was little true synthesis, and even the summary is simply the addition of one response to another. It may be noted, too, that the description, "She's pretty and well built and some good cook at home," was also utilized to describe his daughter.

The tendency to give the first answer that came to mind led to errors, because it was not checked against his total fund of knowledge, although it may not have been completely disconnected from contiguous responses. Discrepancies were not recognized until forced to his attention. The following remarks illustrate the difficulties in leading him through steps normally taken spontaneously and the likelihood of misleading him in the attempt.

"Q. Was Taft president in 1776, 1912 or 1882? F. 1776. Q. Were you alive then? F. Ye—no, I wasn't. Q. Do you remember Taft? F. No. Q. What did he look like? F. A big, fat man. Q. Did you ever see him? F. No—yes. One day in Washington, with my wife. Q. Can you remember him? F. Sure I can. Q. Were you alive then? F. Yes—no, I wasn't. Q. How do you remember him? F. Heard my wife talk of him. Q. I thought you saw him? F. Sure I did. Q. You must

have been alive then. F. Yes—I'd forgotten. Q. When was he president? F. 1776. Q. Were you alive in 1776? F. Yes, sir. Q. What year were you born? F. 1776. Q. How old does that make you? F. Fifty years old. Q. What year is it now? F. 1939—no, I wasn't born then. Q. When were you born? F. (Calculates) March 17, 1881 [incorrect]. Q. Were you alive when Taft was president? F. Yes. Q. When was he president? F. 1914—know damn well he was. Q. 1776, 1882, 1912? F. 1912, I know damn well he was, because I saw him on parade with my wife and daughter."

The automaticity of his responses produced some odd statements. When words adhered to old familiar associations, they occasionally seemed to control the content, instead of being manipulated to suit the occasion. The word, rather than F., was the master. Once, F. was asked what he had done in the carpentry shop during the preceding hour. His reply, "I polished brass" sounded like sheer confabulation. Attention to the accompanying motions along with knowledge of his activities led to the realization that he was using the word "polished" for "sandpapered," and the word "polished" had brought "brass" along with it. At times, such errors controlled the direction of processes of perception and remembering. For example, during a test utilizing the Stanford-Binet [13] picture of Indians paddling a canoe containing a white couple, he called the Indians, "Japanese." Apparently, the total content of the picture did not serve to check the first impression gained from the facial contours. Later, in recalling the picture, he remembered it as a picture of a "Japanese Sandman"; the title of a favorite song taking precedence over proper context.

The salient features of his verbal behavior are summarized.

1. Exclamatory remarks, highly stereotyped phrases and simple confirmatory statements constituted the bulk of his conversation.

2. Normal elaboration did not occur, and direct concrete questioning was required to elicit available information.

3. The content of speech was controlled by old associative bonds in obvious manner.

4. His rapid, unconsidered responses implied that alternatives were not considered.

5. Questions phrased with positive or negative implications led to uncritical affirmation or denial.

6. Synthesis was absent, and responses remained in relative isolation unless brought together for him.

7. He made the minimal effort necessary to satisfy the examiner with virtual absence of self criticism of his responses.

MEMORY FUNCTIONS

The deficiencies and incongruities of F.'s memory were extremely puzzling and led to intensive study. Although F.'s memory, when the term is used in a general sense, was badly disturbed, the deficiencies were found to be similar to those already noted in his general behavior and speech. At first, F.'s ability to utilize the past seemed unpredictable and extremely poor, but he was well oriented and apparently quite aware of recent happenings. Memory for events that had happened after the damage to the brain did not seem notably worse than memory for remote occur-

13. Terman, L. M.: The Measurement of Intelligence, Boston, Houghton Mifflin Company, 1916.

rences. The initial impression that recent events were confused and commingled gave way, on study, to the realization that discrete impressions were retained, but were regained with difficulty.

Recognition remained very good. F. had no difficulty in recognizing persons or surroundings when encountered for a second time. Tests for recognition were performed well. For example, as part of the Babcock test[14] for deterioration, he was required to select 12 picture postcards which he had been shown rapidly after they had been shuffled with 12 similar postcards. His performance was superior, for he selected 9 cards correctly and did not select any cards which he had not been shown before. In recognition, the association is aroused by the immediate stimulus and does not require any spontaneous finding of trends from the past.

The difficulty in eliciting recall lay primarily in the difficulty in setting F. into the proper orientation or channel of association. As noted in the examples of his conversation, the absence of spontaneous elaboration and the tendency to perseverate, or to give positive or negative answers according to the implication of the questions, could be very misleading. When questions were utilized that led him into the appropriate association, it became clear that the material to be recalled had been retained. During the first weeks of study F. was taken on a trip to another hospital, his first leave from the state hospital in more than five years. On the following day it seemed as though the trip had vanished from his memory, but this failure to elicit memories was largely due to the examiner's too ready acceptance of his stereotyped and habitual responses to questions. After several months of study he was taken on a similar trip, and on the following day, by utilizing more suitable questions, it was learned that he recalled details with remarkable accuracy. He was able, for example, to tell the names of members of the party, the procedures carried out, the make of automobile and where he had eaten. To get these responses, it was necessary to use leading questions, but the answers indicated retention of clear visual memories.

A slight hint might suffice to evoke recall, but more often F. had to be led into the proper channel. For example, F. was asked to retell, ten minutes after it had been read to him, the fable about the milkmaid who counted her chickens before they were hatched. The request, "Tell me the story about the milkmaid," only produced the confabulation, "A milkmaid was drinking milk," and the insistence that he could remember no more. When asked to tell "about the milkmaid and a dress," F. was able to retell the story with some degree of adequacy. He no longer floundered when the directional hint was adequate to lead him into the proper association, which he was unable to find unaided. Without direction he was apt to fire the first association that came to mind, which might be a perseveration from a previous response or a habitual association, or to reply simply that he did not know.

The impairment of spontaneous recall must have widespread repercussion when material from the past is unavailable for necessary comparisons, syntheses, and the like. The effect on perception was often noted. When, on viewing pictures in the Stanford-Binet test, he identified the Indians paddling a canoe as "Japanese," it was apparent that the range of associations necessary for proper perception was missing. In similar fashion, he failed to recognize a picture of "Mother Goose" and simply described it literally. He was familiar with "Mother Goose," but the picture did not awaken the proper associations.

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14. Babcock, H.: An Experiment in the Measurement of Mental Deterioration, Arch. Psychol. **24**:117, 1930.

He appeared quite unable to broaden a recollection into full remembrance by the spontaneous arousal of related associations.

The limitations of memory function narrowed the patient's life considerably. Nothing could have full meaning for him. However, the defects seemed essentially similar to those noted in his handling of tasks that were concretely before him, as will be indicated later, and the deficiencies were those noted in his speech and general behavior rather than a specific memory deficit.

TEST PROCEDURES

A very large assortment of procedures was utilized in the examination of the range of F.'s capacities and in analysis of the inconsistencies in his performances. Even though these procedures at first seemed to test for widely divergent mental abilities, the same principles appear to have determined success or failure in almost all tests, and the reader need not be taken through the laborious steps of analysis of all the tests. The discussion will be confined to a relatively small group of examinations which were both typical and critical.

Throughout the studies, careful attention was paid to the demands placed by each item utilized and to the precise conditions under which the test was given. The procedures were considered as controlled samplings of behavior, with greater emphasis placed on F.'s approach and handling of the task than on the scores attained. The tests were repeated or modified as appeared necessary to gain information. The examinations were continued until the formulation of a basic principle permitted a fairly reliable prediction of how F. would handle new tasks.

Several intelligence tests of a general nature were used first, in order to sample F.'s capacities and deficiencies. Further investigations were then pointed at the inconsistencies of his performance; the items on which he fell far below his mean performance and those on which he showed unexpected abilities became the focus of attention. Common denominators were sought among the failures, and also among the successes. When such common factors seemed present, further procedures were sought which would test the hypothesis.

A survey of two intelligence tests, the Stanford-Binet [18] and the Arthur Performance Scale,[15] which actually consist of batteries of tests, will serve as an orientation to the problems involved. In retrospect, careful study of F.'s performances on these two tests goes far toward uncovering the nature of his abilities and disabilities.

On the Stanford-Binet Scale, F. was credited with a mental age of 8½ years, with a base line (success on all items) at the 6 year level and failure on all items at the 12 year level. The Binet test is composed of widely diversified items. Only a few are concerned with ability to solve problems or to think reflectively. Many simply serve to find out whether a child of a given age has learned what the average child has learned at that age. F. was not a child and had learned at least as much as an average adult is supposed to learn. He was often capable of stating information but rarely was able to utilize it. In general, he could gain credit on the items that simply required him to repeat the examiner's example and on those subtests which demanded simple information. He failed where some intelligent utilization of material was necessary. This generalization did not, however, resolve all inconsistencies.

15. Arthur, G.: A Point Scale of Performance Tests, New York, The Commonwealth Fund, 1930.

A typical contrast between success and failure was found in his inability to give simple "differences" at the 7 year level, and his ability to find "similarities" at an 8 year level. He could not tell the difference between "wood" and "glass" and would repeat, "Wood is wood and glass is glass," and, when pressed, "Wood is a hard substance and glass—a female substance." He had no difficulty in telling that "wood and coal both burn." He could not solve the "Ball and Field Test" at the 8 year level, for he would simply draw a line into the circle representing the field and say, "There it is." At the 10 year level he could not recognize any of the simple absurdities but was successful on the "comprehension test." When asked, "Why should we judge a person more by his actions than his words?" he promptly responded, "Because actions speak louder than words."

The performance on the vocabulary items is of special interest because virtually all tests for deterioration are based on Babcock's observation [14] that vocabulary remains relatively well preserved in most patients after organic damage to the brain. Although F. had been a highly competent secretary, and his casual use of words in conversation showed familiarity with highly abstract terms, he could define only 30 words on both lists, a 10 year performance. Even at the 8 year level he could not define objects other than to tell their use. Success or failure did not seem to rest on the degree of abstraction connoted by the word, for he was able to deal with abstract terms readily at times, when a synonym was available.

The spottiness of performance in the Binet test could be partly explained by his ability to utilize knowledge gained at an adult level prior to the damage to the brain, but puzzling problems remained. The Arthur Point Scale of Performance Tests helped to clarify these problems. Performance tests, in contrast to many items of the Binet test, do not measure what the subject had learned in the past. F., as an adult, was not helped much by former acquisitions. On the Arthur Point Scale, F. again showed ability to attain scores on subtests between the mental ages of 6 and 10 years. There were two noteworthy exceptions. On the Healy Completion Test and on the Porteus Maze Test he failed completely, though some degree of success is expected of children between the ages of 5 and 6 years.

The failures on the Healy Completion and the Porteus Maze tests, because of the simplicity of the demands placed by the tests, led to an understanding of F.'s limitations. The simpler Porteus mazes were given repeatedly, with careful instructions. It was clear that F. understood the nature of the task, for he never crossed a line and always continued to emerge at the exit of the maze, but he constantly drew his line into one cul-de-sac after another. No abstract thinking, synthetic ability or marshaling of material from the past is required to complete the task. The failure seemed to lie either in inability to choose between alternative paths or in failure to plan ahead. The Healy Completion Test also sets a simple task, devoid of need for abstract or synthetic abilities. It consists of selecting the appropriate picture blocks from among 50 to fill in the gaps in a picture. F. was unable to select any correctly, even after considerable explanation and illustration. Simplification, by limiting the task to filling one gap and requiring only the choice of the proper block from among 3 blocks, did not lead to success beyond chance performance. F. recognized the correct placement of a block by the examiner and could signify why it was appropriate. His failure seemed to lie in his inability to select from between alternatives. In contrast to the Porteus Maze Test, the need in this test to plan ahead is minimal. He tended to take the first block that came to hand. He was unable to work with alternative choices which would require the imaginative fitting of one block after another—a rapid shifting from the consideration of one potentiality after another until the proper

block for a space was selected. This was very much akin to what F. was unable to do in conversation. The analysis of the failure on the Healy Completion Test led to the recognition of analogous difficulties in other spheres. The inability to cope with alternatives and to shift from one approach to another was then tested in other ways.

It does not seem necessary to examine many of the further samplings of F.'s behavior by test procedures, as the significant features can be indicated in his performances on the Binet and Arthur Point Scale tests. The inability to select between alternatives noted in the Porteus Maze and the Healy Completion Tests served to differentiate between his success and failure on other tests, even when tests appeared to require similar types of mental facility or when they tested widely divergent traits.

It has been noted that F. was able to give similarities between objects, but not differences between them. Giving similarities simply requires the continuation of the same associative trend, e. g., "Wood and coal both burn," whereas giving differences requires shifting to a different trend. At a more complex level, as when one is asked how a book, a newspaper and a teacher are alike, the continuation of a simple single associative trend is not likely to suffice; that is, "book" is not likely to arouse the initial association of "teach." F. could not solve this problem.

It becomes clear why he would be unable to solve the "ball and field test,[11] for success would require imagining alternative placements of the ball and alternative approaches to the solution of the problem.

The ability to perform well on the "comprehension" item at the 10 year level of the Binet test may seem to require a greater capacity for reflection than is needed on some of the simpler tests on which he failed, but it probably takes little reflection for an educated adult to state that one should judge a person by his actions rather than his words, "because actions speak louder than words," for the aphorism has been learned in the past. Perhaps more significant is that the performance requires only the completion of a line of association started by the examiner's words. The question leads him directly into the necessary association, so that no consideration of alternatives and no shift in associational trend is necessary. This hypothesis was tested by means of the "Cameron Test," [16] which requires the completion of a series of phrases ending with "because" and the completion of a similar set of phrases ending in "although." F. could complete phrases ending with "because," such as, "I took a piece of bread because . . .", by adding, "I was hungry"; but he could not complete phrases ending in "although," such as, "I took a piece of bread, although . . ." Although these tasks seem equally simple, phrases ending with "because" require nothing but the completion of a trend already started for him, whereas to complete meaningfully a phrase ending with "although," it is necessary to shift to another trend.

Although the discrepancies in F.'s handling of word definitions cannot be analyzed so clearly, the difference seemed to lie in the same direction. His ability to define a word was not simply a matter of "concreteness" of the word. However, a concrete word connoting an object can be defined by giving the use of the object by means of a single simple association, whereas more "abstract" terms cannot be defined as readily by a simple association unless a synonym is evoked. F. could define objects by giving their use at a simple level. The spottiness in performance was striking because of the occasional definitions at a superior

16. Cameron, N.: Reason, Regression and Communication in Schizophrenics, Psychol. Monog. **50**:1, 1938.

level. When he defined "skill" as "a capability" and "unjust" as "indiscriminatory," he was making only simple associations, no more difficult than using such words as "substance" in conversation. When he defined "charity" as "to give away something you dont want," he was not being facetious or making an epigram. The primary association to the word was quite adequate, but he then followed along a secondary association, which was inappropriate. This type of flaw in association was actually the basis of much of the "frontal humor" he displayed. The assumption that the difficulty in defining words was based on the inability to shift to another trend of association was tried by using Muncie's "Proverb and Metaphor Test."[17] It is necessary to translate into different terms in order to define a metaphor. If the literal trend of association provoked by the metaphor is followed, the definition will be ludicrous. This is precisely what happened. For example, when F. was asked to explain the meaning of "in clover," he produced, "in green pastures"; and he gave the meaning of the term "underdog" as "the dog under him." However, when F. was properly oriented, he could do better. When asked, "If a man were fighting and you said he were the underdog, what would you mean?" he replied, "He was losing the fight." The reason for the "concrete" responses and the difficulty in setting F. in the proper *Einstellung* appears to depend on the inability to shift trends spontaneously.

A still simpler procedure bears out the hypothesis. When asked two meanings of the word "wave," he promptly waved his hand and said, "Hi, Bill!" He could not be induced to give a second meaning spontaneously. It became evident that he knew a second meaning, for when the conversation was shifted to talk of the ocean and he was then asked the meaning of the word "wave," he promptly replied, "A wave on the ocean," accompanying the phrase with an undulating motion of his hand. The same inability was found with a number of simple homonyms. He was able to give the superior definition for the word "tramp" as "a desolated human," but was unable to give a second meaning until asked about marching, when he promptly started to sing, "Tramp, Tramp, Tramp, the Boys Are Marching."

The similarity in the reasons for failure on such simple procedures as the Healy Completion, the Porteus Maze, the Ball and Field, the Cameron and Homonym tests eliminates the necessity of elaborating on the failures in procedures which require synthetic ability, planning ahead, categorical thinking, and the like. Success cannot be anticipated on these more complex tasks when mentation is blocked by the inability to shift associations spontaneously. However, F. sometimes succeeded in tasks which appeared to require considerable intelligence. These superior performances, which at times were more puzzling than his disabilities, require further discussion. The discrepancy between adult ability in some spheres and severe impairment in others has been a stumbling block in the study of behavior in organic deficit states. It appears to have been a major reason for Goldstein's[18] division into tasks which are concrete and those that require ability to deal with the abstract. From this study, the differentiation appears to be simpler and more specific. As has been indicated, superior performances appear to rest on ingrained habit patterns acquired prior to the cerebral damage.

F.'s general level of performance on tests was that of an 8 year old. He could repeat digits, copy drawings, repeat sentences and assemble simple puzzles at this level. He could not achieve even this degree of success when ability to shift to alternative trends of approach was required, as has been discussed. F.'s behavior

17. Muncie, W.: The Psychopathology of Metaphor, Arch. Neurol. & Psychiat. **37**:796 (April) 1937.

18. Goldstein, K.: The Organism, New York, American Book Company, 1939.

differed strikingly in other ways from that of an 8 year old child or of a mentally defective person. Stereotypy, unconsidered responses and facetiousness constituted one side of the differentiation. Still more striking was the large portion of his behavior carried on with a semblance of normal adult manner. He benefited from retention of acquisitions from his normal years and could even add to them to a limited degree. He was not born defective and had assembled a large mass of knowledge and patterned behavior, and these were not wiped out by the damage to his brain, even though they were at times inaccessible. The preservations formed a mask which obscured the severity of the intellectual deficit.

The efforts to teach F. new facilities akin to the superior abilities he displayed accentuated the differentiation between retention and acquisition. Table manners, habits of dressing, courteous and approximately appropriate behavior, remained and are worthy of note. Even though F. defined words poorly, he customarily utilized words which he had always known and, with few exceptions, used them properly, even though the terms were highly "abstract." He sang songs and played the piano, but it was noted that they were all songs he had known prior to the cerebral damage. Although he had formerly been able to play a song after hearing it once, he was now unable to learn how to play a tune despite endless repetition. He could recite a few verses, but efforts to teach him four line jingles met with scant success. He was able to write and reread shorthand, but for a trained stenographer this is no more difficult than reading and writing longhand. Although he could not learn any new manipulations beyond the simplest types of conditioning, as noted in his basketwork and in conditioned reflex tests given by Dr. W. Horsley Gantt,[19] he was able to compose a letter on the typewriter, a skill with which he had been very familiar. Then, too, the letter was written in proper business form, but the contents were stereotyped and jumbled. Even though his card playing was poor, he could play at games of Five Hundred, which had once been a major hobby. He was completely unable to learn a far simpler card game with which he had been unfamiliar. He played at checkers, but could not learn the simpler game of Chinese Checkers, which had become popular after his brain had been damaged. Although it has been maintained[20] that patients with severe intellectual deficits cannot think categorically and cannot group according to categories, F. could separate lists of fruits and vegetables properly and name four or five animals, fruits, colors, etc. Such items had been grouped prior to the injury to the brain. He was unable to form new categories. The differentiation between the ability to form new categories and the ability to handle things according to old groupings was stressed by Vigotsky[21] and led to the formation of his category test, but has been overlooked by many others.

There were a few superior performances not adequately explained. They challenge the hypothesis promulgated. Most striking was F.'s ability to solve two of the three arithmetical problems at the 14 year level on the Binet test. The solution of the problem, "If two pencils cost 5 cents, how many can you get for 50 cents?" may rest on a well learned pattern, but it requires relatively complex mental

19. Gantt, W. H.: Impairment of the Function of Adaptability as Measured by a Simple Conditioned Reflex in Certain Psychogenic as Contrasted with Organic Diseases, South. M. J. **31**:1219, 1938.

20. Nadel, A.: A Qualitative Analysis of Behavior Following Cerebral Lesions, Arch. Psychol. **32**:224, 1938. Weigl, E.: On the Psychology of the So-Called Processes Abstraction, J. Abnormal & Social Psychol. **36**:3, 1941.

21. Vigotsky, L.: Thought in Schizophrenia, Arch. Neurol. & Psychiat. **31**:1063 (May) 1934.

processes. The recording of the mode of solution in the sound film indicated that the performance was automatic: "If two pencils cost 5 cents, how many for 50 cents? If two pencils cost 5 cents, how many for 50 cents? Twenty." It is assumed that such ability is similar to checker playing in that he could work with a well ingrained technic. However, it implies greater plasticity than he has shown in other spheres. In this connection, it is appropriate to note that a school teacher with Pick's disease, whose behavior and performances on tests were even further deteriorated than F.'s, was also able to solve these arithmetical problems without difficulty.

The converse of the preservation of mathematical ability was found in the failure of retention of some items which it had been anticipated had been thoroughly ingrained. The name of the discoverer of America did not rebound automatically, though recognized when offered. F. could not tell anything of "Lincoln" except that he was a president. Even when asked directly whether Lincoln freed the slaves, he mistook "freed" for "feed" and replied, "He fed the slaves rye bread and bologna." Many other such deficiencies in historical data could be cited which are difficult to understand.

In general, the following significant features characterized the patient's test performances:

1. Best performances occurred on tests that rested on past learning or well ingrained habit patterns.

2. Success could be achieved on tests that required repetition alone or completion of a single trend of association started by the examiner, or on performance tests requiring only simple copying or the placement of blocks where no alternative placements were possible because of the shape of the blocks.

3. Virtually no success was achieved on tests which required consideration of alternative approaches, the simultaneous consideration of two trends of association or the spontaneous shifting from one trend of association to another. The failures on the Healy Completion Test, the Porteus Maze Test, the Homonym Test and the inability to complete phrases ending in "although" seem to test different aspects of the same deficiency at the simplest levels possible.

COMMENT

When the mask afforded by the relatively well preserved habitual types of performance was removed, and attention was centered on the capacity for coping with new situations requiring active mentation, the test procedures illuminated this patient's profound deficiency in a basic component of mental activity. F. was found unable to consider alternative approaches to a problem or to shift from one trend of association to another unless specifically guided by an external stimulus. An associational trend when aroused came to an uncomplicated conclusion without leading to another. Consideration of the implications of such disability suggests that his disturbed behavioral pattern can be largely understood on the basis of this defect in mentation.

F.'s spontaneous speech consisted of three types of productions: first, a variety of stereotyped phrases that required no reflection but were habitual remarks preserved from earlier life which vaguely fitted

many situations; second, exclamatory ejaculations, also of an habitual nature, which, even when broadened into a phrase, represented the lowest form of symbolic activity, as pointed out by Hughlings Jackson,[22] and did not express conceptual thoughts, and, third, the simple continuation of a trend started by another person, often merely the affirmation of the intent expressed by another person. There was no synthetic or abstract activity involved in the spontaneous productions, and no ability to shift to a new trend of association on his own initiative.

Verbal responses elicited by questions also consisted, with rare exceptions, of single phrases emitted in rapid, unconsidered, all-or-none fashion. There is no need for pause if no alternatives can be considered. Direct questioning was necessary to elicit very familiar information, for nothing more than the simple association was aroused and this remained unelaborated. The spontaneous perception and correction of inconsistencies in one's statements depend on the ability to summon and compare a broad range of associated material. This was beyond F.'s ability. His speech perseveration also exemplified his failure to shift to new associative trends unless guided by directive questions. When F. said, "I polished brass," instead of "I sandpapered wood," an old established connection provided an association and determined the content of the statement. F.'s pseudohumorous remarks were essentially verbal accidents, often due to improper or unsuited associations bearing a relationship to puns.[23] In the general review of his verbal productions, one could find virtually nothing but simple associations which showed no consideration of alternatives.

Although F.'s memory functions appeared extremely defective, the disturbance could be understood as the result of his inability to regain memories spontaneously through a self-directed chain of associations. He could be led to recall by direct questions. Remembering is an essential part of talking and of spontaneous activity, for the supply of material for intercourse, reflection and autistic processes must arise spontaneously from past experiences.

Most of F.'s daily behavior consisted of patterned activity acquired prior to his incapacitation. These former acquisitions remained potentially available and arose to meet a stimulus from the environment but could be modified only slightly to meet the altered circumstances. The extreme idleness in the state hospital had led observers to the impression that behavior was irreversibly deteriorated. The relative

22. Jackson, J. H.: Notes on the Physiology and Pathology of Language, M. Times & Gaz. **1**:659, 1866; reprinted in Jackson, J. H.: Selected Writings of John Hughlings Jackson, London, Hodder and Stoughton, 1932, vol. 2, p. 121.

23. Jackson, J. H.: An Address on the Psychology of Joking, Brit. M. J., Oct. 22, 1887; reprinted in Jackson, J. H.: Selected Writings of John Hughlings Jackson, London, Hodder and Stoughton, 1932, vol. 2, p. 359.

wealth of activity after transfer to a private clinic provided a striking contrast. It became clear that the apathy and inactivity were not synonymous with inability to be active. The difference in the behavior in the two environments reflected the difference in stimulation and guidance. When the present moment is left in virtual isolation from the past, little other than direct arousal or habit can produce spontaneous behavior. Stimulation dies out rapidly, as it does not produce any chain of inner arousals.

The failure of any breadth of associations impoverished F.'s ability to organize past, present and future into meaningful appreciation of his actual condition or of the situation at any moment. F.'s references to the future were virtually nonexistent, being limited almost entirely to mention of anticipated visits from his wife. The moment seems to have existed in isolation for him, devoid of comparison with the past and of consideration of the morrow. A person without a future differs radically from the normal, as has been fully realized by Freeman and Watts.[8] Without anticipation, anxiety is unlikely, if not impossible. However, euphoria was not the only emotional state that remained possible for F. When the irritation of the moment became great, he responded with appropriate rage; but the rage faded immediately with the passing of the annoyance. Even as anxiety is absent without anticipation, depression may well depend on appreciation of the past. Without ability to compare the present and future with past experience, brooding disappears.

The deterioration of F.'s capacities was partly concealed by his use of ingrained patterns of reactivity. Modes of behavior that expressed basic traits of personality are naturally the most deeply ingrained and are among those best retained; their preservation leads to the continuation of a distinct personality, perhaps to the formation of a caricature of the intact person. In F.'s case some prominent traits disappeared with the occurrence of damage to the brain. The perfectionism in work and the tendency to worry over responsibilities were no longer possible because of the limitations of his associative functioning. On the other hand, the extreme rapidity of his responses may have been simply an exaggeration of his normal behavior. In some ways this tendency toward rapid response may have aggravated his deficiencies by preventing full utilization of whatever small capacities might otherwise have remained available. Other distinctive features of his behavior, such as his pseudoalertness, his good-fellowship, the striving to be the center of attention, the desire to please, were clearly old characteristics carried to extremes and need not be related specifically to dysfunction of the frontal lobe.

The study of the disturbance in F.'s psychologic functioning has led to the rather simple formulation that his associative range was

severely limited by his cerebral lesions, thereby restricting him to the use of those verbal expressions and other reaction patterns immediately stimulated at a given moment, and enormously reducing the associative repercussions of each new incident in his experience, to an extent practically prohibitive of any new learning and producing a bizarre fragmentation of his former intellectual acquisitions, with enough preservation of the well ingrained personality pattern to provide a shell or façade of social personality.

Perhaps as a result of the limitation of his associative range, but quite possibly as the basis for the limitation, his capacity for symbolic activity was shattered. The word, or symbol, as amply illustrated, was no longer a linkage between related experiences. It no longer served as a pivotal point through which a multitude of associations could interrelate. It is suggested that the failure to consider alternatives, to synthesize, abstract or categorize, noted in a variety of deficit states, was in this case due to the failure of words to act as pivots for various associations of the words. The dysfunction due to destruction of the prefrontal lobe is then related to aphasic disorders. Even though the more primary areas and pathways essential to language functioning remain intact, the range of meaning and use of symbols are greatly impaired. There exists paralyzing limitation of symbolic functions, rather than an impediment to their utilization, as in aphasic disorders.

THEORETIC CONSIDERATIONS

The study has been concerned primarily with the endeavor to clarify the nature of the impairment which permitted F.'s bizarre behavior. The observations have led to a theory which is closely related to other theories concerning the nature of impairments of the prefrontal lobe, though expressed in different terms. It is suggested that the formulation of the nature of the defect, particularly when stated in terms of symbolic impairment, permits a unification of various hypotheses which have appeared conflicting.

It is obvious that the overwhelmingly incapacitating defects found in the study of F. have not been noted in other reports of studies of patients with lesions of the prefrontal lobe. Others have not shown a comparable inability to shift from one trend of association to another at a simple level, even if allowances are made for failure of the examiner to differentiate between retained acquisitions and post-traumatic abilities. For example, the description of F.'s behavior cannot be applied to Brickner's [4] patient without considerable modification. The difference, however, may well be a quantitative one. The differences in various patients studied may be a matter of difference in severity of the same type of defect combined with the differences in personality traits of the patients. Various theoretic statements about the effects

of prefrontal lesions are not so divergent when the reasoning behind the statements is examined as might appear simply from reading the summary and conclusions. Although Freeman and Watts,[24] in a recent summary, stated: "We have come a long way from the 'synthesis' of Brickner, and the 'categorical attitude' of Goldstein," the statement may be based on an underevaluation of these concepts.

Bianchi [25] formulated an hypothesis closely related to the theory resulting from the study of F. when he stated:

> Actual impressions succeed one another disconnectedly under the influence of fortuitous external stimuli, and disappear without giving rise to associational processes in varied and recurrent succession. With the destruction of the organ for physiological fusion which forms the basis for association, there disappears also the physical conditions underlying reminiscence, judgment and discrimination.

Grünthal,[26] in a study of a post-traumatic case of what he considered a Korsakov syndrome, but which seemed to resemble more closely a prefrontal than a Korsakov syndrome, found that difficulties arose from "the lack of associational connections between the concept and thought which has just arisen and the total experience—thinking goes on in a single line and necessary collateral connections do not flow into the stream of thought from all sides." Head [27] noted the flaw in associations of a single symbol when he cited the case of a soldier who had sustained a gunshot wound in the left frontal region and who would speak of Boulogne as two different places, the city en route to the front and the city he passed on his return home, and who would write regularly to his mother, though he recognized that she had been dead for two years. Although Goldstein [28] obfuscated his concepts by extending them to cover divergent conditions, and by using the same words with different implications, his most impressive definition of what is "concrete" and what is "abstract" carries a connotation which agrees with the limitations noted in F. He stated:

> In concrete performances a reaction is determined directly by a stimulus—the individual procedure is somewhat passive; as if it were not he who had the

24. Freeman, W. F., and Watts, J.: Psychosurgery, in Spiegel, E. A.: "Progress in Neurology and Psychiatry," New York, Grune & Stratton, Inc., 1946, p. 649.

25. Bianchi, L.: The Mechanism of the Brain and the Function of the Frontal Lobes, New York, William Wood & Company, cited by Brickner.[4]

26. Grünthal, E.: Zur Kenntnis der Psychopathologie des Korsakowschen Symptomenkomplexes, Monatschr. f. Psychiat. U. Neurol. **53**:89, 1923.

27. Head, H.: Aphasia and Kindred Disorders of Speech, London, Cambridge University Press, 1926, vol. 1, pp. 493-494.

28. Goldstein, K.: Human Nature in the Light of Psychopathology, Cambridge, Mass., Harvard University Press, 1940, p. 60.

initiative. In abstract performance an action is not determined by the stimulus but by the account of the situation which the individual gives to himself. The action is more a primary action than a reaction.[28]

This is an acceptable description, even though it is not an explanation, as Goldstein implied it to be. He, like Bianchi and Grünthal, called attention to the observation that the patient's response is bound to the initiating stimulus. Ackerly,[3] in his study of a patient showing minimal defects after frontal lobectomy, noted that she appeared "to have difficulty in registering more than one stimulus at a time." Elder and Miles [29] commented concerning the memory functions of a patient after removal of the left prefrontal regions: ". . . the affection of his memory appeared not so much a blotting out of his past impressions as a want of power of associating memories, of comparing and contrasting them." Though Yarcorzynski and Davis [30] concluded that the frontal lobes are primarily concerned with functions belonging to the field of perception, they noted the "inability of patients to shift readily from one object to another" during tests and commented on the "striking example of the absence of any associative method to remember objects."

Brickner's studies [4] require careful examination, for the fulness of his protocols permits reexamination of the patient's behavior and mental functioning. Whether or not a relationship exists between F's condition and that of Brickner's A. is a critical question. F.'s performances were much poorer than A.'s but presented many similarities. Brickner's concepts have usually been stated too summarily as a "defect in capacity to synthesize." Actually, his analysis of A. led to the summary:

This reduction in synthesizing capacity may reveal itself symptomatically in either of two ways: 1. By manifestations referable to the separate activation of simple engrammatic units which were formerly synthesized. 2. By defects in complex synthesis of simple engrammatic units.

The latter statement is clearly acceptable, for the defect would result from failure to integrate the total situation whatever the cause, and was noted in F. as well as in A. By "separate activation of simple engrammatic units . . . formerly synthesized," Brickner was dealing with faulty utilization of concepts or categories, also stressed by Goldstein. The phrase calls attention to the diminution of associative connections around a concept. Prior to the cerebral damage, the engram had been constructed as a gradual accumulation of associations

29. Elder, W., and Miles, A.: A Case of Tumor of the Left Prefrontal Lobe Removed by Operation, Lancet **1**:363, 1902.

30. Yarcozynski, G. K., and Davis, L.: Experimental Study of Functions of Frontal Lobes in Man, Psychosom. Med. **7**:97, 1945.

around a certain topic bound together by a conceptual symbol. After the damage the associations aroused were limited: the symbol aroused only a portion of the associations previously centering around it. It was compared, contrasted or associated with other engrams in meager fashion.

Brickner's patient, A., in contrast to F., could discuss a topic raised by the examiner with considerable spontaneity. The elaboration seemed excessive at times. However, scrutiny reveals that the elaboration, although profuse, was limited. Some times it was narrowed to a single aspect of the topic, as though following a single trend of association with considerable repetition, without shifting to new associational channels. Sometimes a rather irrelevant association was followed into further irrelevancies, which gave rise to something resembling "flight of ideas": the original topic or concept was lost, rather than remaining the pivotal point of the talk. At other times, a particular aspect of a topic was followed, but it did not broaden into discussion at a conceptual level. The idea, the concept, the total engram, was not handled with sufficient breadth of association to permit shifting to other, related, concepts. Consideration of the performances of Brickner's patient in this manner indicates that his processes of mentation and his utilization of language were clearly limited. The limitation seems related to F.'s difficulties, though at a more complex level of functioning. Here, too, it was concerned with impoverishment of spontaneous interplay between associations and difficulty in shifting from one approach to another. A trend stimulated further associations without external provocation, but only in a limited, direct way, with little brought into consideration from related experiences. Without ability to form greater breadth of associations for pertinent amplification and comparison, remarks and activities are unchecked by accumulated experience, and little new synthesis can occur.

Although careful testing of intelligence has failed to reveal clearcut deficits in many patients with lesions of the prefrontal lobe, there is little doubt that many such patients suffer intellectual impairment of their behavior. Halstead's [31] careful study of a patient failed to reveal any abnormality. The patient was capable of returning to the world of business and advancing rapidly from salesman to president of a corporation. It seemed as though nothing much could be wrong with him. Then the firm went bankrupt because he did not limit his sales orders to capacity for production—an obvious defect in his ability to consider all of the essentials, rather than following along a single line of thought and

31. Halstead, W.: Brain Injuries and the Higher Levels of Consciousness in Trauma of the Central Nervous System, A. Research Nerv. & Ment. Dis., Proc. **24**:480, 1945.

activity. Although at an extremely complicated level, this patient's behavior seems to follow in line with the simpler defects noted in F., in Brickner's patient and by many other investigators. Intelligence tests have not been constructed to distinguish impoverishment of the breadth of higher associations.

Because this type of defect is a matter of limitation rather than of impediment, its disturbance of mental functions is not obvious. Man can function fairly well even without the full range of his associative capacities, particularly when assets attained prior to the cerebral damage remain relatively intact and at his disposal. Behavior beyond the habitual is demanded relatively infrequently.

Freeman and Watts,[8] from their extensive experience with patients following frontal lobotomy, are clearly cognizant that some deficiency results. They have paid most attention to the patient's inability to project himself into the future and to the hypothesis that severance of the connections between the frontal lobes and the thalamus lessens the emotional component of abnormal behavior. Freeman, however, has recently made an unusually clear statement of the perspective presented in this paper, although he apparently does not consider it sufficient to explain the changes in behavior noted in patients. He said:

> There probably is a permanent reduction in the richness of the associations which enables a person to see all the implications of the questions and his replies. In other words, the patient after lobotomy seems to finish his thinking more quickly and with greater satisfaction to himself than the normal person.[32]

As has been amply indicated in this study, such reduction in richness of association constitutes a defect in intelligence; and consideration of the consequences of this defect seems to explain the abnormalities of behavior which were observed in our patient. The divergence in results of lobotomy according to placement of the sectioning lends credence to the idea that more posteriorly placed sections produce a greater limitation of associations and an impairment of the functioning dependent thereon almost as severe as noted in F.

SUMMARY

The study reported has emphasized the importance of a severe limitation in associative range as a determinant of the behavioral disturbance after damage of the prefrontal regions. The hypothesis is offered, on the evidence from this case study, that symbolic activity is affected after damage to the prefrontal lobe because of the diminution in ability to shift from one associational trend to another. It is considered possible that the limitation of associations and the ensuing

32. Freeman, W.: In Discussion on Freeman, W., and Watts, J. W.: Psychosurgery: 1936-1946, Arch. Neurol. & Psychiat. **57**:770 (June) 1947.

degradation of behavior are dependent on the failure of symbols as links with or pivots for related experiences. Although it has been clear that lesions producing aphasia disrupt symbolic activity at more primary levels, the limitation of associative range and of the use of symbols following lesions of the prefrontal regions has not been so apparent. Such limitations may not be noted readily both because of the diversity and breadth of human facilities and because the limitations are masked by knowledge and behavioral patterns acquired prior to damage to the brain. In some cases, as in F.'s, the intellectual defect is obvious. In other cases in which the impairment is slight, little may be noted other than some degree of shortsightedness—an absence of consideration of the total circumstances and prior experience. As stated by Freeman, the thinking is finished more quickly and with greater satisfaction and assurance than in normal persons. In all cases of dysfunction due to lesions of the prefrontal lobes it may be that symbols, although readily available, are deprived of their full associative value, and that this limitation may affect the ability to utilize other assets.

Johns Hopkins Hospital (5).

COMBINED LATERAL AND VENTRAL PYRAMIDOTOMY IN TREATMENT OF PARALYSIS AGITANS

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IN RECENT years there has been great interest in the surgical treatment of parkinsonism, following the work of Bucy and Case,[1] in 1939, which demonstrated that it was possible to relieve tremor by operative means. Previously it had been shown that the medical treatment of paralysis agitans was unsatisfactory. There had been long experience with various drugs, primarily those of the atropine series, which provided only transient and slight relief. The inadequacy of medical measures necessitated a more radical approach, which in the past ten years has produced a variety of surgical technics.

Meyers [2] set up criteria for an ideal operative procedure for the relief of tremor, of which the following are important:

1. The benefits to be anticipated from the operation should be commensurate with the risks involved.

2. No impairment of function beyond that already in evidence should result from the operative procedure. Ideally, the operation should not leave the patient with permanent paresis, dyspraxia, diminution of intellect, aphasia, incoordination or disturbance of sensation.

3. The operation should be devised so as to deal, if possible, with all three major feateures of paralysis agitans—tremor, rigidity and poverty of movement.

4. The procedure should be technically standardized so that results are consistent in the hands of different surgeons.

5. The operation should be applicable to cases of bilateral involvement.

6. It should be possible to deal with symptoms of both sides of the body at one operation.

From the Beth Israel Hospital.

Read at the meeting of the New York Society of Neurosurgery, May 18, 1948.

1. Bucy, P. C., and Case, T. J.: Tremor: Physiologic Mechanism and Abolition by Surgical Means, Arch. Neurol. & Psychiat. **41**:721-746 (April) 1939.

2. Meyers, R.: The Modification of Alternating Tremors, Rigidity and Festination by Surgery of the Basal Ganglia, A. Research Nerv. & Mental Dis., Proc. (1940) **21**:602-665, 1942.

PREVIOUS OPERATIVE PROCEDURES

The surgical procedures in use at present may be divided into three groups on the basis of anatomic level of approach: those involving (1) the cortex, (2) the basal ganglia and (3) the spinal cord.

The cortical procedures are, in part, based on the observation of Parkinson [3] in one of his cases that generalized tremor at rest was abolished on the right side during the time that that side was paralyzed as the result of a cerebral vascular accident. This observation was confirmed by Patrick and Levy [4] in 1927 and by Balser [5] in 1942. Aring and Fulton [6] demonstrated in the monkey that cerebellar tremor could be relieved by extirpation of the precentral cortex. With this background, Bucy and Case,[1] in 1939, excised areas 4 and 6 on the left side for relief of right-sided tremor following a severe head injury. This produced complete relief of tremor, although speech and motor function were temporarily impaired. Putnam,[7] in 1940, excised area 6 on the right side for treatment of tremor in the left forearm and hand. Tremor was diminished in severity but not eliminated, and a mild paresis ensued. Klemme [8] had a wide experience with excision of the premotor cortex in cases of paralysis agitans and athetosis.

After considerable research into the anatomy and physiology of the precentral cortex, Bucy [9] came to the conclusion that the impulses transmitting tremor travel specifically in the posterior part of the precentral gyrus in area 4 γ; the Betz cells, from which the large fibers of the pyramidal tract arise, are located in this strip. He, therefore, in 1945, excised area 4 γ in a patient with right-sided tremor affecting both the upper and the lower extremity. Tremor at rest was abolished immediately, without return in a period of sixteen months after operation.

3. Parkinson, J.: An Essay on the Shaking Palsy, London, Sherwood, Neely & Jones, 1817.

4. Patrick, H. T., and Levy, D. M.: Parkinson's Disease, Arch. Neurol. & Psychiat. **7**:711-720 (June) 1922.

5. Balser, B. H.: Alternating Tremor and Its Relation to Cortical Pathways, Arch. Neurol. & Psychiat. **47**:962-970 (June) 1942.

6. Aring, C. D., and Fulton, J. F.: Relation of the Cerebrum to the Cerebellum: II. Cerebellar Tremor in the Monkey and Its Absence After Removal of the Principal Excitable Areas of the Cerebral Cortex (Areas 4 & 6a, Upper Part); III. Accentuation of Cerebellar Tremor Following Lesions of Premotor (Area 6a, Upper Part), Arch. Neurol. & Psychiat. **35**:439-466 (March) 1936.

7. Putnam, T. J.: Treatment of Unilateral Paralysis Agitans by Section of the Lateral Pyramidal Tract, Arch. Neurol. & Psychiat. **44**:950-976 (Nov.) 1940.

8. Klemme, R. M.: Surgical Treatment of Dystonia, Paralysis Agitans and Athetosis, Arch. Neurol. & Psychiat. **44**:926 (Nov.) 1940.

9. Bucy, P.: Surgical Relief of Tremor at Rest, Ann. Surg. **122**:933-941, 1945.

Meyers [10] has done much work on surgery of the basal ganglia. In 1940 he reported his results following extirpation of the head of the caudate nucleus and interruption of certain extrapyramidal fibers in the region of the anterior limb of the internal capsule. Six of 8 patients showed various degrees of improvement.

In the spinal cord, the anterolateral column was cut by Foerster and Gagel,[11] without producing any definite change in symptoms. Putnam [12] performed anterolateral chordotomy in 5 cases of unilateral tremor of paralysis agitans, without success. Mashanskiy [13] reported permanent recovery in 3 and satisfactory results in 5 of a series of 17 patients subjected to cervical anterolateral chordotomy. Oldberg [14] sectioned the anterolateral column in 2 cases of unilateral postencephalitic tremor, without result. Pollock and Davis [15] cut several posterior roots in a case of rigidity and tremor of one upper extremity. Rigidity was diminished but not tremor. The column of Burbach was cut by Puusepp [16] in a case of paralysis agitans affecting one upper extremity. Rigidity was decreased but not tremor. In 1940 Putnam [7] performed section of the lateral pyramidal tract in the upper cervical portion of the cord for relief of unilateral tremor. There was considerable relief of tremor in all his cases, and loss of motor power was less than might have been expected. In this procedure, an incision 4 mm. in depth was made in the posterolateral column at the level of the second cervical segment, between the line of the posterior roots and the dentate ligament. Tribromethanol or pentobarbital sodium anesthesia was used. In cases in which the abnormal involuntary movements interfered with the operation ether was employed.

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10. Meyers, R.: A Surgical Procedure for Postencephalitic Tremor with Notes on the Physiology of the Premotor Fibers, Arch. Neurol. & Psychiat. **44**:455 (Aug.) 1940.

11. Foerster, O., and Gagel, O.: Die Vorderseitenstrangdurchschneidung beim Menschen, Ztschr. f. d. ges. Neurol. u. Psychiat. **138**:1-92, 1932.

12. Putnam, T. J.: Results of Treatment of Athetosis by Section of Extrapyramidal Tracts in the Spinal Cord, Arch. Neurol. & Psychiat. **39**:258-275 (Feb.) 1938.

13. Mashanskiy, F. I.: Traitement chirurgical des mouvements involontaires des extrémités appliqué au parkinsonisme post-encéphalitique, J. de chir. **46**:877-899, 1935.

14. Oldberg, E., in discussion on Putnam.[12]

15. Pollock, L. J., and Davis, L.: Muscle Tone in Parkinsonian States, Arch. Neurol. & Psychiat. **23**:303-319 (Feb.) 1930.

16. Puusepp, L.: Cordotomia Posterior Lateralis (Fasc. Burdachi) on Account of Trembling and Hypertonia of the Muscles in the Hand, Folia neuropath. estoniana **10**:62-66, 1930.

PATHWAYS FOLLOWED BY IMPULSES PRODUCING TREMOR

In considering the problem of the surgical treatment of tremor and rigidity, it is most important to determine the neural pathways through which the impulses producing these disorders travel. With this information it would be possible to select the most advantageous surgical site at which to interrupt these impulses. In our understanding of the tracts involved, we have been almost completely dependent on the information obtained from surgical experiment on human victims of the disease. Information of this type is difficult to check and permits much subjective interpretation. It is therefore necessary to study critically the available information compiled by various investigators.

Certain anatomic and physiologic facts are basic to this investigation. Area 4 in man is divisible into three parts—area 4 γ, area 4 a and area 4 s, all of which probably contribute to the pyramidal tract. The human pyramid just rostral to the decussation contains roughly about a million nerve fibers, of which 61 per cent are myelinated and the rest unmyelinated. Of the myelinated fibers, 90 per cent are 1 to 4 microns, approximately 7 per cent are 5 to 9 microns and approximately 2 to 3 per cent are more than 9 microns, in diameter. It is from the large Betz cells of area 4 γ that the large pyramidal fibers, greater than 9 microns, arise. The remaining fibers that make up the pyramidal pathways are believed to arise from areas 4 a and 4 s, from an indefinite portion of the parietal lobe and possibly from area 6.

The pyramidal pathways in man consist of a large crossed lateral bundle, the lateral corticospinal tract; a small uncrossed lateral bundle, the ventrolateral corticospinal tract, and an extremely variable uncrossed anterior bundle, the ventral corticospinal tract. The degree of decussation is more variable in the human brain than in the brain of other primates. Flechsig,[17] in 1876, found in his series of human brains some with large lateral and negligible ventral pyramidal tracts and others with large ventral and small lateral tracts.

The lateral corticospinal pathway runs the length of the cord, and the ventrolateral corticospinal pathway may. The ventral corticospinal tract is believed to terminate in the thoracic region, although in some cases it may be traced to the lower lumbar region. The lateral pathway terminates in the anterior gray column of the same side, whereas the ventrolateral and ventral tracts cross to the gray column of the opposite side.

As mentioned earlier, Aring and Fulton demonstrated in monkeys that tremor produced by section of the superior cerebellar peduncle

17. Flechsig, P.: Die Leitungsbahnen im Gehirn und Rückenmark des Menschen auf Grund entwicklungsgeschichtlicher Untersuchungen, Leipzig, Wilhelm Engelmann, 1876.

could be eliminated by section of areas 4 and 6. Bucy and Case excised areas 4 and 6 in man, with complete abolition of tremor. Putnam showed that removal of area 6, with area 4 intact, would only partially relieve tremor. More recently, Bucy demonstrated that excision of area 4 γ alone, in the posterior part of the precentral gyrus, from which the Betz cells and the large fibers of the pyramidal tract arise, produces complete elimination of tremor. Putnam's experiences with cervical posterolateral chordotomy have shown that at least some of the impulses producing tremor and rigidity travel in the posterolateral column. The important descending tracts in this area are the lateral corticospinal, the rubrospinal and the lateral reticulospinal. Although it is conceivable that the rubrospinal and lateral reticulospinal tracts are implicated in the transmission of tremor, in view of Bucy's experience with excision of area 4 γ, it seems likely that it is in truth the interruption of the lateral pyramidal tract that has been essential to the relief of tremor and rigidity. Bucy [9] has therefore formulated the theory that tremor is transmitted from the Betz cells of area 4 γ through the large fibers of the pyramidal tract, and that destruction of the substantia nigra, or of the globus pallidus, or of both, is the commonest lesion which releases the pyramidal system to this form of abnormal hyperactivity.

CONSIDERATIONS IN PROPOSED PROCEDURE

The difference in the results following Bucy's section of area 4 γ, in which there was complete cessation of tremor, and Putnam's section of the posterolateral column, in which there was partial relief of tremor, may possibly be attributed to the fact that lateral pyramidotomy does not interrupt all the fibers arising from the large Betz cells of area 4 γ. It seemed likely, therefore, that more complete relief of tremor by the spinal cord approach might be achieved by section of the ventral corticospinal pathway in addition to section of the lateral corticospinal. In view of the fact that at the level of the upper cervical portion of the cord the lateral pyramidal tract has already made its crossing and the ventral corticospinal pathway has yet to do so, the contemplated procedure entailed section of the lateral corticospinal tract on one side and of the ventral corticospinal tract on the opposite side.

As seen in figure 1 *A*, the lateral corticospinal tract, lying in the posterolateral column, is easily sectioned. The incision in the cord used by Putnam for lateral pyramidotomy is shown in figure 1 *B*. Interruption of the opposite ventral corticospinal tract is more difficult, in view of its position in the posteromedial portion of the anterior column, alongside the anterior sulcus. The ventral tract might be reached in one of two ways: (1) by direct incision of the anterior white column, a proceedure which is difficult and would necessarily

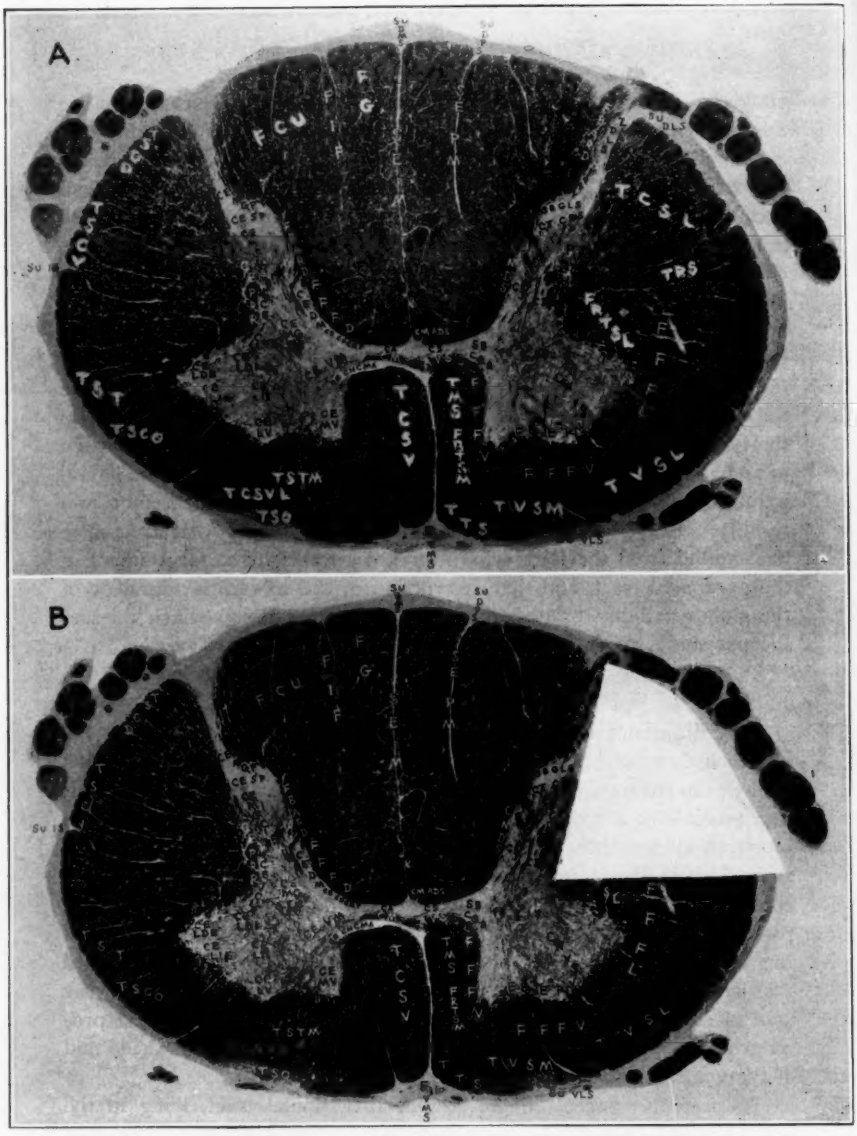

Fig. 1.—*A,* cross section of the spinal cord at the level of the fifth cervical segment. (From Riley, H. A.: An Atlas of the Basal Ganglia, Brain Stem and Spinal Cord, Baltimore, Williams and Wilkins, 1943.) *B,* cross section of the spinal cord at the level of the fifth cervical segment, demonstrating section of the posterolateral column for interruption of the lateral pyramidal tract. *FCU,* indicates fasciculus cuneatus; *FG,* fasciculus gracilis; *FRTSL,* lateral reticulospinal tract; *FRTSM,* medial reticulospinal tract; *TCSL,* lateral corticospinal tract; *TCSV,* ventral corticospinal tract; *TCSVL,* ventrolateral corticospinal tract; *TMS,* mesencephalospinal tract; *TRS,* rubrospinal tract; *TSCD,* dorsal spinocerebellar tract; *TSCO,* spinocollicular tract; *TSCV,* ventral spinocerebellar tract; *TSO,* spino-olivary tract; *TST,* lateral spinothalamic tract; *TSTM,* medial spinothalamic tract; *TTS,* tectospinal tract; *TVSL,* lateral vestibulospinal tract; *TVSM,* medial vestibulospinal tract.

destroy most of its other tracts; (2) by cross incision from the opposite side, as demonstrated in figure 2, with the advantage that it would thus be possible to section the lateral corticospinal tract of one side and the ventral corticospinal tract of the other through one incision, with relatively little unnecessary interruption of pathways.

Examination of specimens of the upper cervical portion of the cord indicated that this section could be accomplished by insertion of the blade in the line of the posterior roots at an angle of approximately 20 degrees with the vertical. The depth of incision required was 8 to 9 mm., the tip of the blade then being withdrawn in the line of the

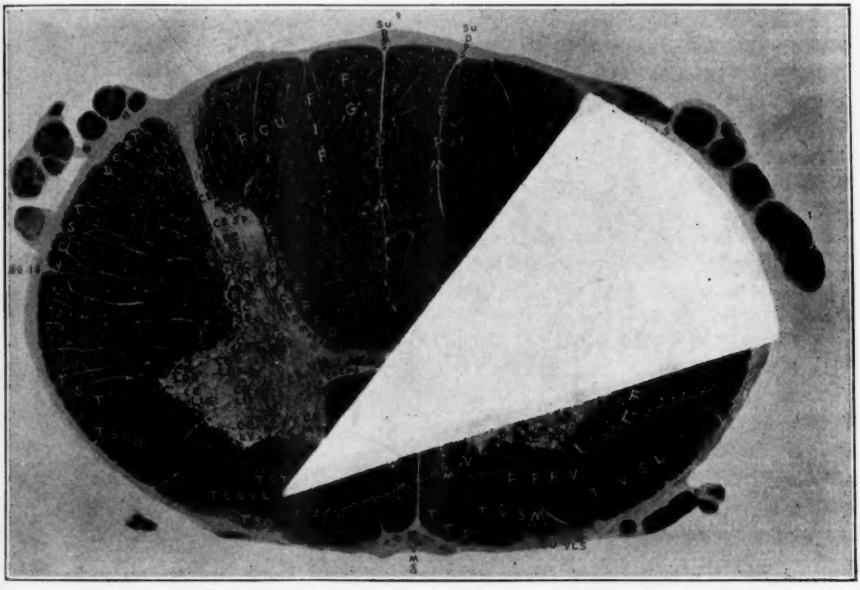

Fig. 2.—Cross section of the spinal cord at the level of the fifth cervical segment, demonstrating area sectioned in combined lateral and ventral pyramidotomy.

dentate ligament on the side of insertion. This procedure is shown in figure 3.

In performing a chordotomy of this extent, several problems must be considered: 1. Would an incision of this extent permit the return of any motor function? 2. Might the anterior spinal artery be damaged, with resulting hemorrhage? 3. Might damage to blood vessels, even if not of a degree sufficient to produce significant hemorrhage, result in inadequate tissue nutrition and cause degeneration of the cord?

In order best to determine the depth of incision required, it was decided to carry out the procedure with local anesthesia, using the states of tremor, rigidity and voluntary power as criteria.

It is convenient to have a short term by which to describe an operative procedure. The area sectioned is not a specific anatomic region. It is true that many pathways are cut, but since the purpose of the procedure is to section the lateral and ventral corticospinal tracts, a reasonably accurate description would be "chordotomy for interruption of the lateral pyramidal and the opposite ventral pyramidal tracts." Such a title, however, would be unwieldy. Therefore, with full understanding that many other pathways are incidentally severed, "combined lateral and ventral pyramidotomy" is suggested as a descriptive title.

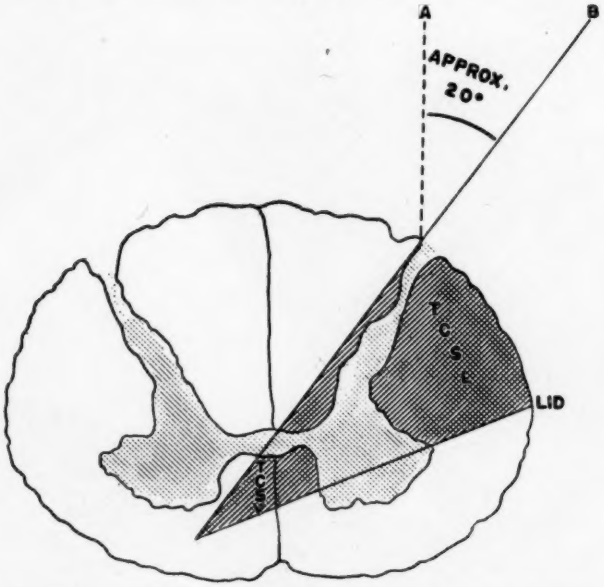

Fig. 3.—Diagram illustrating technic of combined lateral and ventral pyramidotomy. *TCSL*, lateral corticospinal tract; *TCSV*, ventral corticospinal tract; *LID*, dentate ligament; *B*, line of incision, at angle of approximately 20 degrees with the vertical, *A*; depth of incision, 8 to 9 mm.

REPORT OF CASES

The present series is composed of 11 cases in which combined lateral and ventral pyramidotomy was performed. Of these, 3 are of special interest

Case 1.—J. R., a man aged 29, was admitted to Beth Israel Hospital on Oct. 16, 1946. At the age of 10 years he had had headache, nausea, vomiting, fever and diplopia, followed by weakness and awkwardness of the right hand. This was followed shortly by the appearance of tremor and rigidity in the right upper and lower extremities. With the passage of time, shortening of the right upper and lower extremities became apparent.

Of interest in the physical examination was the shortening of the right extremities. Neurologic examination disclosed hemiplegic gait involving the right side and coarse, rapid, alternating tremor of the right extremities, more pronounced in the upper. Tremor of the upper extremity was so severe that the patient found it necessary to sit on the hand and forearm to control it. Muscle strength in the right extremities was almost normal except for the hand and fingers, which could not be used because of flexion contracture. Muscle tone in the right extremities was greatly increased. Deep reflexes were hyperactive on the right. Hoffmann and Babinski signs were elicited on the right. Paralysis of the left oculomotor nerve was noted.

Operation.—On October 19, with the use of local anesthesia, laminectomy at the level of the second, third and fourth cervical vertebrae was performed. The posterolateral column on the right, between the fourth and fifth cervical segments, was incised to a depth of 4 mm., sufficient to interrupt the lateral pyramidal tract, without eliminating tremor, rigidity and voluntary movement. The incision for combined lateral and ventral pyramidotomy was performed to a depth of 8 mm., after which there was immediate cessation of violent tremor in the upper and lower extremities on the right side and complete, flaccid paralysis of these extremities.

Bladder control appeared on the third day. Motor power began to return on the sixth day. The patient was able to walk at the time of his discharge from the hospital, two and one-half weeks after operation. Motor power reached its maximum in approximately three months.

At the time of this report, there has been a follow-up period of twenty months. Tremor at rest is no longer present except under the influence of extreme emotion. Tremor on movement is present, but it is much less severe than that noted before operation. Muscle tone in the right upper and lower extremities is almost within the limits of normal. Muscle strength in the right lower extremity is similar to that observed before operation. Motor power in the right upper extremity has returned to approximately 90 per cent of its preoperative level. The patient is now doing manual labor.

This experience was of interest, as it demonstrated the following points:

1. Section of the lateral pyramidal tract alone does not immediately eliminate tremor, rigidity and voluntary movement.

2. Section of the lateral pyramidal tract and the opposite ventral pyramidal tract results in immediate disappearance of tremor, rigidity and voluntary movement.

3. Combined lateral and ventral pyramidotomy produces great relief of tremor and rigidity, without regression over a considerable length of time.

4. After the combined procedure there is a quite satisfactory return of motor power.

5. Hemorrhage in or degeneration of the spinal cord need not result.

CASE 2.—J. K. was admitted to Beth Israel Hospital on Jan. 21, 1948. He had been well until two and a half years before admission, at which time tremor in the right extremities appeared, followed gradually by the presence of the same symptom in the left extremities, the tremor being of greater severity in the upper

limbs than in the lower and much severer on the right side than on the left. At first there was no rigidity, but approximately four months before admission this condition appeared. Weakness and slowness of movement had also been noted. Various medicaments, including scopolamine, had been taken, without relief.

Examination revealed fine, rapid, alternating tremor of both upper extremities, being of much greater severity on the right. Tremor of less severity was observed in both lower extremities. Gait was propulsive. There was slight rigidity in the right upper extremity. Masked facies was noted.

Operation.—On January 23 combined right lateral and left ventral pyramidotomy was performed between the fourth and the fifth cervical segment. The depth of incision was 8 mm. There was immediate disappearance of tremor, rigidity and voluntary power in the right extremities. Bladder function returned on the fifth day. The patient was able to raise the right upper extremity on the fourth postoperative day.

It is now four months since operation. Tremor at rest on the right side is absent except during moments of stress. Tremor on movement may occur, but it is of much less severity than that noted before operation. Motor power on the right is 35 to 40 per cent of the preoperative strength, but it is not hampered by rigidity and tremor. Movements on the right side are smoother and more easily initiated. The patient can walk unassisted. He is now ready for light work.

This case has been presented because it demonstrates a rather typical course and result. There have been better and worse results.

CASE 3.—D. L., aged 40, a former instructor in English at Johns Hopkins University, was admitted to Beth Israel Hospital on Nov. 4, 1947. Twelve years before his admission tremor in the right hand was observed. Rigidity developed in the right upper and lower extremities and then appeared in the opposite limbs. In the preceding months speech had become "slurring" in character. The patient had taken belladonna, use of which had to be discontinued because of vomiting. Examination revealed flexion contractures of the fingers and hands on both sides. There was rigidity of great degree in the musculature of all extremities. Because of rigidity, practically no movement was possible, although it was obvious that there was much latent motor power. Mild and only occasional tremor was seen in the hands and fingers, being greater in the right than in the left.

Operation.—On November 6, with the use of local anesthesia, a combined right lateral and left ventral pyramidotomy was performed between the fourth and the fifth cervical segment. The depth of incision was 8 mm. After operation, tremor of the right hand and fingers disappeared and rigidity was greatly improved. Movements of the right extremities became possible, with much greater facility in the initiation of activity. Improvement on the right side has persisted up to the time of writing.

This case is of interest because it demonstrates that the procedure is also of benefit in cases in which rigidity and difficulty in initiation of movement, rather than tremor, are the prime symptoms.

LATERAL AND VENTRAL PYRAMIDOTOMY

Technic.—Preoperative medicaments are pentobarbital sodium U. S. P. and morphine sulfate. For local anesthesia, procaine hydrochloride, 1 per cent, alone

is used until the cordotomy has been performed. After this thiopental sodium U. S. P. (pentothal sodium®) is administered.

Before operation the anesthetist makes a careful check of the side to be operated on for tremor, muscle tone and voluntary power, in order to have a basis for comparison following section of the cord. Often, as the result of preoperative medication, tremor and rigidity disappear. It has, however, been found that in the absence of two of the criteria the remaining one is reliable, so that if tremor and rigidity are no longer present at the stage of incision of the cord the motor state is a satisfactory guide.

In the usual fashion, the spinous processes and laminas of the second, third and fourth cervical vertebrae are removed, with greater exposure on the side of section. The dura is opened off the midline to the side of section. The arachnoid is incised in order to empty partially the subarachnoid space. An area in the posterolateral column, free of blood vessels, between the fourth and the fifth cervical segment, is selected for section. This level is preferred in order that there may be no interference with the innervation of the phrenic nerve, which receives its main supply from the fourth cervical segment. The dentate ligament is identified and held tightly with long forceps in order to brace the cord during incision. A long-handled center point cataract knife with a total length of 7⅛ inches (15.1 cm.) is used. This can be constructed by any instrument maker. A distance of 8 mm. is marked off on the blade with bone wax. The instrument is inserted into the cord in the line of the posterior roots at an angle of approximately 20 degrees with the vertical. It is best to become familiar with the proper angle by practice on a postmortem specimen of the cervical portion of the cord, using the smallest angle with the vertical which will cross the midline and sever the opposite ventral pyramidal tract. The depth of incision is 8 mm., the tip of the blade being drawn out at the dentate ligament. The extremities are then observed for cessation of tremor, loss of rigidity and paralysis. If necessary, the incision is deepened very slightly. The maximum depth required has been 9 mm. When the section is complete, cessation of tremor, loss of rigidity and paralysis in both extremities of the side of operation are observed.

Postoperative Course.—Urinary retention appears immediately after operation. Tidal drainage is therefore instituted on the patient's return from the operating room. Normal bladder control appears, on the average, on the fifth day or sixth day. Bowel function is aided by cathartics and enemas. The usual care of the skin is provided.

Paralysis has lasted, on the average, from eight to ten days, after which time there is gradual return of function. Function may return first in either the upper or the lower extremity, proximally or distally. Physical therapy, which is begun on the fifth day, includes heat, massage, passive and active exercises, reeducational exercises and sine wave stimulation.

The patient is out of bed, in a chair, on the fourteenth day and is then gradually encouraged to stand and walk. The average period of hospitalization is four weeks. Physical therapy is continued for five months after operation, treatments being given four to five times weekly.

Complications.—Certain complications were encountered in the course of this procedure:

1. There were several infections of the bladder, which responded without great difficulty to treatment with drugs.

2. Pain in the shoulder on the side of operation, lasting from several days to several months, was a frequent complaint. It was

thought that pain might be due to damage inadvertently done to posterior rootlets. In subsequent cases, particular care was taken to avoid these structures. Nonetheless, the symptom continued to recur. It may well be the result of damage within the cord to nerve fibers of the posterior root or to the cells of the gray column.

3. Pain and temperature sensibility was lost on the opposite side, usually in the lower extremity but occasionally more extensively. In some cases it cleared up after a few months; in others the loss was permanent. This was, of course, the result of section of some of the fibers of the lateral spinothalamic tract.

4. A psychiatric reaction characterized by negativism occurred in 1 case.

5. A postoperative hemorrhage from the wound occurred in 1 case; it was controlled. Wound healing thereafter was uneventful.

Results.—In 11 cases operation was performed for relief of symptoms on one side. In 3 of these, the picture was that of unilateral paralysis agitans, with involvement of both sides in the other 8. In 2 of the 8 cases with bilateral involvement, severe symptoms were present on one side with only slight involvement of the other side.

Of the 11 cases, tremor and rigidity were present in 5 and tremor without rigidity in 4; in 1 case rigidity was the prominent symptom, with only rare and slight tremor, and in another there were rigidity and flexion contractures of the forearm and leg on one side, without tremor.

In no case in this series did tremor affect the facial musculature. It was observed, however, that all patients with rigid facies showed relaxation of facial muscles and greater mobility of expression after relief of rigidity resulting from the operation.

Tremor and Rigidity: In the 5 cases with tremor and rigidity, tremor at rest has practically disappeared. It may exist in moments of emotional stress. Intention tremor has been seen in 2 of these cases, but it is of much less severity than that noted before operation. Rigidity in these 5 cases has been greatly reduced, so that muscle tone is close to normal.

Tremor Without Rigidity: In the 4 cases of tremor without rigidity, tremor at rest was eliminated, except for twitching of the thumb in 1 case. Slight intention tremor was noted in 2 of these cases.

Rigidity: In the case in which rigidity was a prominent symptom with mild tremor in the background, there were great relief of rigidity and disappearance of tremor on the side of operation. In the case with rigidity of the left side and flexion contractures of the left forearm and leg, without tremor, the abnormal muscle tone was greatly reduced immediately after operation, and, with physical therapy, the flexion contractures were almost completely straightened out. The patient

returned home after operation and died of unknown cause two and one-half months after the operation had been performed. This death was the only one in the series.

Bladder Function: As mentioned earlier, bladder control appeared on the fifth or sixth postoperative day. There was no subsequent dysfunction of the bladder in any of these cases.

Motor Power: In 2 cases there was very poor return of motor power, perhaps no more than 20 per cent. The disease was far advanced in both cases, and the patients left the hospital one week after operation because of the pressure of hospital bills. The patients were from out of town, and the quality of the physical therapy received is open to question. In 1 case motor power returned to 90 per cent of its preoperative level. In the remaining cases, motor power returned, on the average, to approximately 35 to 40 per cent of that noted before operation.

It is important to emphasize that in the cases in which rigidity was presented there was, usually, before operation a considerable amount of latent motor power which could not be utilized because of hypertonus of muscle. After the procedure, with decrease in rigidity, considerable improvement in motor status was observed. Movements were more freely performed, and through a greater range, even though there was actually less strength. Therefore, in situations in which rigidity is prominent the procedure actually results in greater effective motor power. Poverty of movement, which is characteristic of these patients, is thus considerably relieved.

Permanence of Results: The neurologic status tended to stabilize within approximately three months after operation. In the longest follow-up observation of any case of this series, one year and eight months, there has been no change since the third postoperative month, and relief of tremor and rigidity has been maintained. This has been true of all the cases in this series.

Social Adjustment: This may be considered in terms of rehabilitation and relief of symptoms.

(*a*) Rehabilitation: One patient does heavy work; 1 patient conducts a hobby shop together with his wife; 2 of the patients recently operated on will soon be able to take on light work.

(*b*) Relief of symptoms: All the other patients are more comfortable, with tremor and/or rigidity relieved. They are able to participate in the life of the family to a greater degree. In this group, the major problem is a financial one. The patients with means are able to construct a fairly satisfactory life. For those without means it is much more difficult.

COMPARISON OF RESULTS OF COMBINED LATERAL AND VENTRAL PYRAMIDOTOMY IN MAN WITH SECTION OF THE PYRAMIDS IN ANIMALS

It may be of interest to compare the neurologic results of this procedure with the results following the experimental section of the pyramid in animals. It is understood, of course, that many tracts besides the pyramidal are damaged in this procedure.

Tower,[18] in an experimental study of unilateral lesions of the pyramid in the monkey, observed that muscle tone was diminished and that tendon reflexes were slow and full. Superficial reflexes were lost. Defective initiation and execution of all performance by the skeletal musculature and elimination of all discrete use of the digits were observed. In the chimpanzee, hypotonia and paresis appear, of which the latter is more prominent. The paresis is of the same type as that seen in the monkey, but the defect is greater because discrete use of the digits is of greater importance in the normal activity of the chimpanzee.

Neurologic examination following combined lateral and ventral pyramidotomy demonstrated, in the majority of cases, a rather normal muscle tone. Muscle strength was reduced, on the average, to 35 to 40 per cent of that noted before operation, with, as observed in primates, greater loss in the discrete use of the fingers. Hyperactive deep reflexes were present with spread, and Babinski and Hoffmann sign were usually, but not always, elicited. Loss of pain and temperature sensation, particularly in the lower extremities of the opposite side, was frequently observed. Sensory loss was permanent in some cases and transitory in others.

USE OF COMBINED LATERAL AND VENTRAL PYRAMIDOTOMY IN CASES OF BILATERAL INVOLVEMENT

There is as yet no record in the literature of a cortical operation performed for the relief of bilateral symptoms in paralysis agitans. Putnam referred, however, to a personal communication from Klemme in which he mentioned a bilateral cortical procedure.

Bucy and Fulton [19] and Bieber and Fulton [20] demonstrated in animal experiments that bilateral extirpation of the precentral region results in the abolition of all voluntary muscular activity and complete incapacitation of the animal. It does not necessarily follow that the same result will occur in man, but it seems quite likely that a bilateral cortical procedure would not be feasible.

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18. Tower, S. S.: Pyramidal Lesion in the Monkey, Brain **63**:36-90, 1940.

19. Bucy, P. C., and Fulton, J. F.: Ipsilateral Representation in the Motor and Premotor Cortex of Monkeys, Brain **56**:318-342, 1933.

20. Bieber, I., and Fulton, J. F.: Relation of the Cerebral Cortex to the Grasp Reflex and to Postural and Righting Reflexes, Arch. Neurol. & Psychiat. **39**:433-454 (March) 1938.

The possibility of utilizing the combined lateral and ventral pyramidotomy for relief of bilateral symptoms was then considered. The procedure would necessarily entail a considerable section of the cord, as demonstrated in figure 4. Since the manner in which motor function is provided to the extremities which have been deprived of their innervation from the pyramidal tract is not definitely known, the gravest problem to be faced in contemplating a bilateral procedure was the possibility that it might leave the patient without motor innervation below the level of incision. It was therefore of considerable interest to study the results of bilateral lesions of the medullary pyramids in

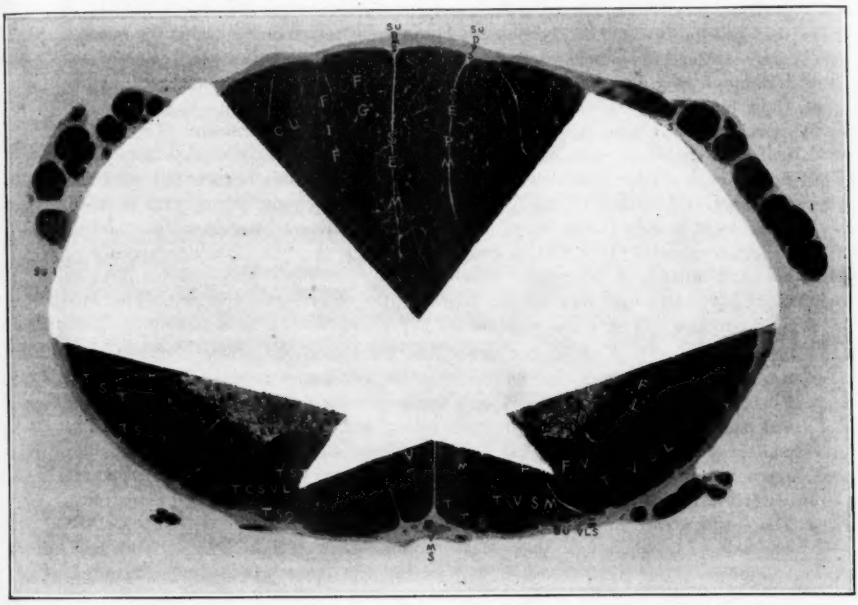

Fig. 4.—Cross section of the spinal cord at the level of the fifth cervical segment, demonstrating areas sectioned in combined lateral and ventral pyramidotomy performed on both sides.

animals, it being recognized, of course, that the situations were not truly comparable. Tower [18] has demonstrated in monkeys that bilateral lesions produce on both sides the symptoms and signs observed after unilateral destruction. The motor defect, however, is made more prominent by the animal's need to use paretic muscles in performing movement rather than the muscles of the intact (opposite) side. Whereas with a unilateral lesion the hypotonia is more pronounced in the extremities and abdomen than in the rest of the trunk, a bilateral lesion extends the defect almost equally to the axial musculature. It is believed that

the involvement of trunk muscles following bilateral section is due to loss of function of the ventral corticospinal path. It has been observed that discrete use of the neck musculature is not possible, with resulting inability to turn, elevate or depress the head independently of the body. These experiments suggested that combined lateral and ventral pyramidotomy, performed bilaterally, might permit the retention of some degree of motor power, and that in the case of far advanced disease, in a bedridden patient, its experimental use might be warranted.

The opportunity soon arose to test the feasibility of this double procedure.

CASE 4.—Dr. N. M., aged 46, had formerly been a member of the faculty of the Carnegie Institute of Technology. He entered Beth Israel Hospital on June 24, 1947. He had been well until seven years before admission, when tremor of the left upper and lower extremities was observed. Tremor then appeared in the right upper and lower limbs and rapidly became very severe. Rigidity of all extremities was then noted and gradually became very prominent. The patient had been unable to walk unassisted for five years, and even with assistance could take very few steps, and only with the greatest hesitancy. Speech was faint and indistinct. Of interest in the past history was an episode of influenza in 1918. Neurologic examination revealed fine, rapid, alternating tremor of all extremities, of great severity. This was more pronounced on the left. Extreme rigidity of all extremities was observed. Practically no movement was possible because of rigidity, although considerable latent motor power was apparent. The face was immobile and devoid of expression.

Operation.—On June 26, combined right lateral and left ventral pyramidotomy was performed between the fourth and fifth cervical segments. The depth of incision was 8 mm. This section was followed by immediate cessation of tremor and flaccid paralysis of the right extremities. Bladder control appeared approximately on the tenth postoperative day. Movements of the right extremities appeared on the twelfth postoperative day. After three months there was moderate power, with smoothness of movement in the right upper and lower extremities. There was great reduction in rigidity. Tremor was entirely absent. The patient was able to take approximately 30 steps unassisted.

However, the rigidity and tremor of the left upper and lower extremities, particularly the rigidity in the left hand and fingers, was so disturbing that the patient demanded relief. The dangers of a double procedure and the fact that it had not been performed before were presented to the patient and his family, who decided, nonetheless, to have it done. Therefore, on December 19, approximately four months after the first operation, combined left lateral and right ventral pyramidotomy was performed between the fifth and the sixth cervical segment, one segment below the level of the first incision. The depth of incision was 8 mm. This procedure was followed by immediate cessation of tremor and disappearance of rigidity in the left extremities. Of interest was the fact that there was no diminution in the strength of the right extremities. On the evening following operation the patient was able to raise the left upper extremity. Bladder control appeared in approximately four weeks. Routine postoperative care was administered. The patient left the hospital five weeks after operation.

On April 30, 1948, approximately ten months after the first operation and four months after the second, the patient was completely free of tremor in all extremities. Rigidity was greatly reduced throughout, and muscle tone was approximately

normal in all four limbs. The patient was able to move all his extremities freely and smoothly. He could walk well with assistance and was able to climb stairs. It was estimated that he walked approximately 400 steps a day. The patient was able to sit up in a chair for an indefinite period and spent almost his entire day either sitting or walking. He was able to read and turn the pages of a book unassisted. It was also possible for him to feed himself. Moving pictures have been taken demonstrating these points.

IDENTIFICATION OF TRACTS SECTIONED IN PROCEDURE

The purpose of the procedure is to section the lateral and the opposite ventral pyramidal tracts. In order to accomplish this, numerous other pathways must be interrupted.

TABLE 1.—*Combined Lateral and Ventral Pyramidotomy*

Interrupted Tracts on One Side	Interrupted Tracts on Opposite Side
Descending	
Lateral corticospinal	Ventral corticospinal
Portion of ventral corticospinal	Mesencephalospinal
Rubrospinal	Medial reticulospinal
Lateral reticulospinal	
Mesencephalospinal	
Ascending	
Dorsal spinocerebellar	None
Ventral spinocerebellar	
Portion of lateral spinothalamic	
Portion of fasciculus gracilis	
Portion of fasciculus cuneatus	

TABLE 2.—*Combined Lateral and Ventral Pyramidotomy Performed Bilaterally*

Interrupted Tracts on Each Side	
Descending	**Ascending**
Lateral corticospinal	Dorsal spinocerebellar
Ventral corticospinal	Ventral spinocerebellar
Rubrospinal	Portion of the lateral spinothalamic
Lateral reticulospinal	Portion of fasciculus gracilis
Medial reticulospinal	Portion of fasciculus cuneatus
Mesencephalospinal	

The tracts sectioned on the two sides of the cord as the result of the incision for the combined lateral and ventral pyramidotomy are listed in table 1. The pathways sectioned in the course of the double procedure are listed in table 2.

CONCLUSIONS AS TO PATHWAYS FOLLOWED BY IMPULSES PRODUCING TREMOR AND RIGIDITY

May any conclusions concerning the pathways for tremor and rigidity be reached from the experiences with combined lateral and ventral pyramidotomy? It is obvious that when numerous pathways are interrupted results cannot be interpreted with absolute certainty in terms of damage to one set of tracts. However, the relief of tremor

following this chordotomy, in which the lateral pyramidal tract of one side and the ventral pyramidal tract of the other have been sectioned, suggest that Bucy's theory, of the transmission of impulses producing tremor through the Betz cells of area 4γ and the large fibers of the pyramidal tracts, is correct.

The experiences reported here suggest that impulses producing rigidity travel in the pyramidal tracts of the spinal cord. Nothing, of course, can be said about its cerebral pathway.

RETURN OF MOTOR POWER FOLLOWING PROCEDURE

The method of transmission of impulses for voluntary movement after section of a relatively large portion of the spinal cord, including the ventral and lateral corticospinal tracts, must now be considered. The experiences of investigators with section of the pyramids in the monkey and chimpanzee have prepared one to expect some return

TABLE 3.—*Combined Lateral and Ventral Pyramidotomy Performed Bilaterally*

Uninterrupted Tracts on Each Side	
Descending	**Ascending**
Ventrolateral corticospinal	Most of fasciculus gracilis
Medial vestibulospinal	Most of fasciculus cuneatus
Lateral vestibulospinal	Medial spinothalamic
Tectospinal	Most of the lateral spinothalamic
Olivospinal	Spinocollicular
	Spino-olivary

of function following a lesion which includes the pyramidal tracts. The amount of residual motor power after operation in the cases presented here, particularly in the one in which the double procedure was carried out, is perhaps greater than might have been expected.

Lassek's [21] investigations into the functions of the pyramidal tract are of interest at this point. In a series of 106 cases in which hemiplegia was present during the patient's life, as the result of brain tumor or cerebral vascular accident, autopsy revealed complete destruction of the pyramid in only 7. In 37 cases there was partial destruction. In 63 cases with clinical evidences of hemiplegia no changes in the pyramid were seen on gross or microscopic study. These observations suggest that, although the pyramidal tracts are of importance, they occupy a less vital position in the transmission of motor impulses than has heretofore been thought.

21. Lassek, A. M.: The Human Pyramidal Tract: A Study of the Pyramids in Cases of Acute and Chronic Vascular Lesions of the Brain, Arch. Neurol. & Psychiat. **54**:339-343 (May) 1945.

With the pyramidal tracts gone, how are motor impulses transmitted? The remaining intact pathways after the double procedure are listed in table 3. Of the descending tracts, only the ventrolateral corticospinal and the medial and lateral vestibulospinal tracts are known with certainty to extend all the way to the lumbar region of the spinal cord. It is also conceivable that there are effective motor fibers in the ascending pathways.

Nonetheless, the tracts enumerated seem inadequate to the transmission of impulses for the motor power demonstrated in the case of the double procedure. It may be, therefore, that the present concept of function of the spinal cord, in terms of the transmission of specific types of impulses through separate and discrete pathways, is faulty, and that spinal cord action is better conceived as the response of an integrated unit to impulses from above.

RELATIVE MERITS OF THE CORTICAL OPERATION AND COMBINED LATERAL AND VENTRAL PYRAMIDOTOMY

The advantages of the cortical operation are these:

1. In cases of symptoms in the upper extremity it is possible to resect the cortical representation of the upper limb without damaging the innervation of the lower extremity. This is not feasible in the procedure on the spinal cord.

It is known that there is no topographic arrangement of fibers, in terms of upper and lower extremity, in the medullary pyramid. It is not clear, however, whether there is such an arrangement in the various pyramidal tracts of the cord. Nonetheless, it is not likely that a differential section of the pyramidal tracts for relief of symptoms of the upper extremity alone can be performed.

2. A second advantage of the cortical operation is that relief of facial tremor is possible.

The advantages of combined lateral and ventral pyramidotomy are these:

1. Symptoms in the lower extremity are more easily managed. The cortical motor representation of the lower extremity is exposed only with difficulty.

2. The landmarks are clearcut and objective, which is not true in the cortical approach.

3. Motor function is better preserved.

4. Aphasia and convulsions do not follow the procedure.

5. The method can be used in the treatment of bilateral paralysis agitans, whereas a bilateral cortical operation does not appear to be feasible.

APPLICATION OF COMBINED LATERAL AND VENTRAL PYRAMIDOTOMY TO TREATMENT OF PARALYSIS AGITANS

Up to the present, the surgical treatment of paralysis agitans has been limited primarily to the treatment of unilateral tremor alone. The procedure of combined lateral and ventral pyramidotomy makes it possible to provide relief for almost all types of paralysis agitans, whether early or late. It may be used in the relief of tremor alone, in the relief of tremor and rigidity or in the relief of rigidity alone—whether the symptoms are unilateral or bilateral.

The single operation is beneficial in cases of unilateral symptoms and in those cases of bilateral disease with severe involvement of one side and little involvement of the other. At first the procedure was not used except in cases of advanced disease for fear that the patient's motor status might be impaired. It has since become clear that the early cases with relatively good voluntary movement show the best results in terms of postoperative motor function. In the cases of bilateral disease in which one side alone is severely damaged it is surprising how much benefit may be obtained from the single procedure. Therefore, in cases which qualify for single section, that is, those with unilateral involvement or with bilateral disease more prominent on one side, operation may and should be done relatively early.

The double procedure should be reserved for cases with severe involvement of both sides. What results may be expected from the procedure? In the advanced cases in which the double operation is necessary, the aim is to eliminate or decrease the distressing symptoms of tremor and rigidity. It may be possible to provide the patients with greater facility in the use of their arms and hands and to enable them to walk. They may be able to leave their beds and take a greater part in family life, but they cannot be returned to useful life or made independent of assistance. In short, they can be made considerably more comfortable and happy, but they will continue to require care.

In those cases with unilateral disease or with bilateral disease severe on one side only, in which the single procedure is applicable, relief of symptoms may, of course, be anticipated. Tremor and rigidity can be relieved and moderate motor function produced. The patients may be able to care for their own needs and get about unassisted. In addition, some of these persons may be rehabilitated and returned to a useful life.

It might be of interest, finally, to see how well the procedure of combined lateral and ventral pyramidotomy stands up against the

criteria set up by Meyers for an ideal surgical procedure for the relief of tremor.

1. Benefits to be anticipated from operation should be commensurate with the risks involved.

They are commensurate with the risks involved.

2. No impairment of function beyond that already in evidence should result from the operative procedure. Ideally the operation should not leave the patient with a permanent paresis, dyspraxia, diminution of intellect, aphasia, incoordination or disturbance of sensation.

This procedure results in a slight to moderate degree of paresis and, occasionally, in loss of pain and temperature sensation on the opposite side of the body. Diminution of intellect, aphasia and incoordination do not occur.

3. The operation should be devised so as to deal, if possible, with all three major features of paralysis agitans—tremor, rigidity and poverty of movement.

This procedure does deal with all three major features of the disease. It does not, however, relieve tremor of the face.

4. The procedure should be technically standardized so that results are consistent in the hands of different surgeons.

This procedure is technically standardized because of the anatomic landmarks available.

5. The procedure should be applicable to cases of bilateral involvement.

It is applicable to cases of bilateral disease.

6. It should be possible to deal with symptoms of both sides of the body at one operation.

It may well be possible to deal with symptoms of both sides of the body at one operation.

SUMMARY

1. A new surgical technic for the treatment of paralysis agitans is presented. In this procedure, combined lateral and ventral pyramidotomy, the lateral pyramidal and the opposite ventral pyramidal tract are sectioned through a single incision in the cord.

2. Use of this procedure in the treatment not only of tremor, but of rigidity and poverty of movement as well, is demonstrated in a series of 11 cases.

3. One case is presented in which combined lateral and ventral pyramidotomy was performed bilaterally, with good result.

4. Application of this procedure to the treatment of the major symptoms of paralysis agitans affecting one side or both sides is discussed.

CEREBRAL LESIONS RESPONSIBLE FOR DEATH OF PATIENTS WITH ACTIVE RHEUMATIC FEVER

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IN SOME cases of severe rheumatism nervous symptoms are so prominent that the condition is called "cerebral rheumatism." In 1845 Hervez de Chégoin [1] described 3 cases of such a disease. These and similar observations were recorded by Trousseau,[1] Sydenham,[2] Girard,[3] Leyden,[4] Telgmann [5] and other authors in the nineteenth century. In the great modern clinical treatises, the only cerebral complication of rheumatism mentioned is chorea; however, the old observations of the French clinicians have never been forgotten, and many monographs have since been published on cerebral rheumatism, among them those of Rosenthal and Joffe [6]; Hoppe [7]; Williams [8]; Coombs [9]; Toulouse, Marchand and Courtois [10]; Mørch-Christensen [11]; Foster,[12] and Castex.[13] Psychiatric observations on the encephalic complications of

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1. Cited by Enriquez, E., and Weil, M. P., in Enriquez, Laffitte, Laubry and Vincent: Tratado de patología interna, Salvat Editores, Barcelona, 1927.

2. Sydenham, cited by Girard.[3]

3. Girard: Thèse de Paris, 1862.

4. Leyden, E.: Zwei Fälle von acuter Bulbärparalyse, Arch. f. Psychiat. **7**:44, 1877.

5. Telgmann, J.: Toxämische Delirien bei Herzkranken, Deutsche med. Wchnschr. **25**:305, 1899.

6. Rosenthal and Joffe, cited by Winkelman and Eckel.[89]

7. Hoppe, H.: Cerebral Rheumatism, Lancet-Clinic **105**:219, 1909.

8. Williams, E. M.: Cerebral Rheumatism, New York M. J. **94**:478, 1911.

9. Coombs, C.: Cerebral Rheumatism, Practitioner **88**:99, 1912.

10. Toulouse, E.; Marchand, L., and Courtois, A.: Rheumatisme aigu cérébral: Considérations anatomo-pathologiques, Bull. et mém. Soc. méd. d'hôp. de Paris **47**:1119, 1931.

11. Mørch-Christensen, A.: Myelitis Developing as Sequel of Rheumatic Fever, Hospitalstid **81**:327, 1938.

12. Foster, D. B.: Association Between Convulsive Seizures and Rheumatic Heart Disease, Arch. Neurol. & Psychiat. **47**:254 (Feb.) 1942.

13. Castex, M. R.: Reumatismo cerebral crónico, Prensa méd. argent. **30**:1401, 1943.

rheumatism have been published by Haskell,[14] Dunlap,[15] Bumke,[16] Bleuler,[17] Bouman,[18] Bender,[19] Froment and Brun [20] and Dublin.[21] In the same manner, Juster, [22] Fahr,[23] Console [24] and others noted clinical manifestations of encephalic lesions in their general studies on rheumatic fever. Special reference must be made to Bruetsch,[25] who in his many publications insisted on a close relation between rheumatism and many severe mental diseases. Almost all the authors here cited have agreed in describing late pictures of insidious onset and chronic evolution as the most prominent cerebral symptom of rheumatism, considering them as sequelae rather than as direct manifestations of the disease.

In all these clinical papers there is a notable uniformity of criteria in regard to the relation of the cerebral symptoms to the anatomic lesions in the fine vessels of the meninges and of the cerebral cortex.

14. Haskell, R. H.: Mental Disturbances Associated with Acute Articular Rheumatism, Am. J. Insanity **71**:361, 1914.

15. Dunlap, C. B.: Dementia Praecox: Some Preliminary Observations on Brains from Carefully Selected Cases, and a Consideration of Certain Sources of Error, Am. J. Psychiat. **80**:403, 1924.

16. Bumke, O.: Die Auflösung der Dementia praecox, Klin. Wchnschr. **3**:437, 1924.

17. Bleuler, E. P.: The Physiogenic and Psychogenic in Schizophrenia, Am. J. Psychiat. **87**:203, 1930.

18. Bouman, K. H.: De Schizophrenie als organische hersenziekte, Nederl. tijdschr. v. geneesk. **75**:2564, 1931.

19. Bender, L.: Psychiatric, Neurologic and Neuropathologic Studies in Disseminated Alterative Arteriolitis, Arch. Neurol. & Psychiat. **36**:790 (Oct.) 1936.

20. Froment, R., and Brun, J.: Myoclonies survenues au decours d'une crise de rhumatisme articulaire aigu: encéphalite rhumatismale "a minima," Lyon méd. **157**:587, 1936.

21. Dublin, W. B.: Pathologic Lesions of the Brain Associated with Chronic Rheumatic Endocarditis and Accompanied by Psychosis, Dis. Nerv. System **2**:390, 1941.

22. Juster, I. R.: The Significance of Rheumatic Activity in Chronic Rheumatic Heart Disease, Am. Heart J. **15**:1, 1938.

23. Fahr, T.: Beiträge zur Frage der Herz- und Gelenkveränderungen bei Gelenkrheumatismus und Scharlach, Virchows Arch. f. path. Anat. **232**:134, 1921.

24. Console, A. D.: Relation of Cardiac Lesions to the Clinical Course of Rheumatic Fever, Arch. Int. Med. **69**:551 (April) 1942.

25. Bruetsch, W. L.: Psychosen bei chronischer Endokarditis, Psychiat.-neurol. Wchnschr. **38**:551 and 563, 1936; The Histopathology of the Psychoses with Subacute Bacterial and Chronic Verrucose Rheumatic Endocarditis, Am. J. Psychiat. **95**:335, 1938; Chronische rheumatische Gehirnerkrankung als Ursache von Geisteskrankheiten: Eine klinisch-anatomische Studie, Ztschr. f. d. ges. Neurol. u. Psychiat. **166**:4, 1939; Chronic Rheumatic Brain Disease as a Possible Factor in the Causation of Some Cases of Dementia Praecox, Am. J. Psychiat. **97**:276, 1940; Rheumatic Endarteritis of Cerebral Vessels: Sequel of Rheumatic Fever, Tr. Am. Neurol. A. **68**:17, 1942; Rheumatic Epilepsy: Sequel of Rheumatic Fever, Am. J. Psychiat. **98**:727, 1942; Late Cerebral Sequelae of Rheumatic Fever, Arch. Int. Med. **73**:472 (June) 1944. Rheumatic Brain Disease: Late Sequel of Rheumatic Fever, J. A. M. A. **134**:450 (May 31) 1947.

In fact, in the brains of rheumatic patients vascular lesions are frequently observed; meningeal hemorrhages, cerebral embolism, cerebral purpura and edema had been studied in 1863 by Ollivier and Ranvier,[1] and their observations were soon confirmed by Martin [26]; and Krehl [27]; Hanot [28]; Simmonds [29]; de Mussy, Legroux and Astier,[30] and Rabé.[31] These lesions are variants in the general picture of proliferative inflammation, which in general narrows the finer arterioles and produces multiple small foci of ischemia, localized principally in the cerebral cortex. Similar types of proliferative endangiitis were soon described not only in cases of rheumatism but also infectious diseases independent of rheumatism and of intoxications; Hayem,[32] and Landouzy and Siderey [33] observed them in cases of typhoid; Huguenin,[34] in cases of diphtheria, and Jores,[35] in cases of lead poisoning.

Special importance is attributed to the work of Nissl [36] and Alzheimer,[37] who demonstrated the exact nature of what the former called syphilitic endarteritis of small cortical vessels, a condition which is frequently observed in syphilitic patients but which is similar microscopically to the vascular lesions of rheumatism, to many infectious diseases and to some intoxications. Alzheimer made a thorough study of the consequences of cerebal ischemia due to proliferation of the arterial

26. Martin, H.: Récherches sur la nature et la pathogénie des lésions viscérales consécutives a l'endartérite oblitérante et progressive (scléroses dystrophiques). Rev. de méd. **1**:369, 1881.

27. Krehl, L.: Beitrag zur Pathologie der Herzklappenfehler, Deutsch. Arch. f. klin. Med. **46**:454, 1890.

28. Hanot, V.: Considérations générales sur le rhumatisme articulaire aigu, Presse méd. **2**:171, 1894.

29. Simmonds, H.: Ueber Hirnblutung bei verruköser Endocarditis, Deutsche med. Wchnschr. **27**:353, 1901.

30. de Mussy, Legroux and Astier, cited by Rabé.[31]

31. Rabé, M.: Contributions a l'étude des lésions des artères dans l'infection rhumatismale, Presse méd. **10**:927, 1902.

32. Hayem, G.: Récherches sur les rapports existant entre la mort subite et les altérations vasculaires du cœur dans la fièvre typhoïde, Arch. de Physiol. norm. et path. **2**:699, 1869.

33. Landouzy, L., and Siderey, A.: Contribution a l'histoire de l'artérite typhoïdique, Rev. de méd. **5**:843, 1885; Étude des localisations angiocardiques typhoïdiques, ibid. **7**:804 and 919, 1887.

34. Huguenin, P.: Contribution a l'étude de la myocardite infectieuse diphtérique, Rev. de méd. **8**:790 and 995, 1888.

35. Jores, L.: Ueber die pathologische Anatomie der chronischen Bleivergiftung des Kaninchens, Beitr. z. path. Anat. u. z. allg. Path. **31**:183, 1902.

36. Nissl, F.: Zur Histopathologie der paralytischen Rindenerkrankungen, in Nissl, F., and Alzheimer, A.: Histologie und histopathologie. Arbeiten über die Grosshirnrinde, Jena, G. Fischer, 1921, vol. 1, p. 315.

37. Alzheimer, A.: Progressive Paralyse und endarteritische Hirnlues, Centralbl. f. Nervenh. u. Psychiat. **16**:443, 1905.

intima. According to this author, when the vascular lesions are slight, there are only discrete alterations of the neurons, such as cloudy swelling, whereas when the focal ischemia is severe there appear cortical areas devoid of nerve cells and without important reactive phenomena (*Verödungsherde*, or areas of devastation), and even miliary softenings (*Erweicherungsherde*).

Since these reports, observations on endarteritis and ischemic foci in the brain have multiplied, so that now their frequency, their morphologic variability and their low specificity are established. For a more detailed discussion on this problem, the publications of Von Glahn and Pappenheimer,[38] Winkelman and Eckel,[39] Bodechtel [40] and Karsner and Bayless [41] should be consulted. These papers contain many original data, as well as exhaustive and well discussed bibliographies.

It is now known that the vascular lesions of rheumatism affect the peripheral and visceral systems, as well as the cerebral vessels; lesions have also been noted in the aorta, the coronary vessels and the pulmonary artery. These lesions are found in profuse distribution both in the acute and in the chronic stage of the disease, thus leading to the conclusion that rheumatic fever is a disease which involves the entire circulatory system.

The majority of authors believe that the vascular lesions of rheumatism are nonspecific; however, a few have related them to rheumatic disease. Thus, Aschoff,[42] Coombs [43] and Wätjen [44] observed specific nodules in the adventitial and medial layers of the coronary arteries; Pappenheimer and Von Glahn [45] and Barnard,[46] in the adventitial layers

38. Von Glahn, W. C., and Pappenheimer, A. M.: Specific Lesions of Peripheral Blood Vessels in Rheumatism, Am. J. Path. **2**:235, 1926.

39. Winkelman, N. W., and Eckel, J. L.: The Brain in Acute Rheumatic Fever: Nonsuppurative Meningo-Encephalitis Rheumatica, Arch. Neurol. & Psychiat. **28**:844 (Oct.) 1932.

40. Bodechtel, G.: Gehirnveränderungen bei Herzkrankheiten, Ztschr. f. d. ges. Neurol. u. Psychiat. **140**:657, 1932.

41. Karsner, H. T., and Bayless, F.: Coronary Arteries in Rheumatic Fever, Am. Heart J. **9**:557, 1934.

42. Aschoff, L.: Zur Myokarditisfrage, Verhandl. d. deutsch. path. Ges. **8**:46, 1904.

43. Coombs, C.: The Histology of Rheumatic Carditis and Other Rheumatic Phenomena, Brit. M. J. **1**:620, 1911.

44. Wätjen, J.: Ein besonderer Fall rheumatischer Myokarditis, Verhandl. d. deutsch. path. Gesellsch. **18**:223, 1921.

45. Pappenheimer, A. M., and Von Glahn, W. C.: Lesions of the Aorta Associated with Acute Rheumatic Fever, and with Chronic Cardiac Disease of Rheumatic Origin, J. M. Research **44**:489, 1923-1924; Studies in the Pathology of Rheumatic Fever: Two Cases Presenting Unusual Cardiovascular Lesions, Am. J. Path. **3**:583, 1927.

46. Barnard, W. G.: Diffuse and Nodular Fibrosis of Adventitia of Aorta (Rheumatic Periaortitis), J. Path. & Bact. **32**:95, 1929.

of the aorta; MacCallum,[47] Sacks,[48] von Sántha,[49] Coburn [50] and Craciun, Visineanu and Ursu [51] stated the belief that the multiple thrombosis and the hemorrhages are due to a primary vascular disease; Rössle [52] stated that vascular lesions are part of the general reaction of the mesenchyma, and Karsner and Bayless [41] asserted that the fibrinoid necrosis in the wall of the vessels is suggestive, but insufficient for determining the specificity of the lesions; in this point, they follow the criterion of Fahr [53] and Metz,[54] in contradiction to that of Swift,[55] Swift, Derick and Hitchcock,[56] Klinge,[57] Klotz and Lloyd,[58] Semsroth and Koch [59] and Apitz.[60]

According to all the authors, the vascular lesions in the brain of rheumatic patients are followed by few local secondary alterations. Besides, the morphologic features of these lesions are very similar to

47. MacCallum, W. G.: Rheumatism, J. A. M. A. **84**:1545 (May 23) 1925.

48. Sacks, B.: The Pathology of Rheumatic Fever: A Critical Review, Am. Heart J. **1**:750, 1925-1926.

49. von Sántha, K.: Ueber Gefässveränderungen im Zentralnervensystem bei Chorea rheumatica, Virchows Arch. f. path. Anat. **287**:405, 1932.

50. Coburn, A. F.: Relationship of the Rheumatic Process to the Development of Alterations in Tissues, Am. J. Dis. Child. **45**:933 (May) 1933.

51. Craciun, E. C.; Visineanu, N., and Ursu, A.: Les lésions histologiques de la maladie de Bouillaud; leur valeur biologique, Ann. d'anat. path. **10**:157, 1933.

52. Rössle, R.: Zum Formenkreis der rheumatischen Gewebsveränderungen, mit besonderer Berücksichtigung der rheumatischen Gefässentzündungen, Virchows Arch. f. path. Anat. **288**:780, 1933.

53. Fahr, T.: Die rheumatische Granulomatose (rheumatisches Fieber, Rheumatismus infectiosus specificus, Rheumatismus verus) von Standpunkt des Morphologen, Ergebn. d. inn. Med. u. Kinderh. **54**:357, 1938.

54. Metz, W.: Die geweblichen Reaktionserscheinungen an der Gefässwand bei hyperergischen Zuständen und deren Beziehungen zur Periarteritis nodosa, Beitr. z. path. Anat. u. z. allg. Path. **88**:17, 1931.

55. Swift, H. F.: The Pathogenesis of Rheumatic Fever, J. Exper. Med. **39**:497, 1924.

56. Swift, H. F.: Derick, C. L., and Hitchcock, C. H.: Rheumatic Fever as a Manifestation of Hypersensitiveness (Allergy or Hyperergy) to Streptococci, Tr. A. Am. Physicians **43**:192, 1928.

57. Klinge, F.: Das Gewebsbild des fieberhaften Rheumatismus: I. Das rheumatische Frühinfiltrat (akutes degenerativ-exsudatives Stadium), Virchows Arch. f. path. Anat. **278**:438, 1930; II. Das subakut-chronische Stadium des Zellknötchens, ibid. **279**:1, 1931; Der Rheumatismus: pathologisch-anatomische und experimentell-pathologische Tätsachen und ihre Auswertung für das ärzliche Rheumaproblem, Ergebn. d. allg. Path. u. path. Anat. **27**:1, 1933.

58. Klotz, O., and Lloyd, W.: Sclerosis and Occlusion of the Coronary Arteries, Tr. A. Am. Physicians **45**:108, 1930.

59. Semsroth, K., and Koch, R.: Ueber Gefässlesionen bei Allgemeininfektion; ein Beitrag zur Genese der Periarteritis nodosa, Krankheitsforschung **8**:191, 1930.

60. Apitz K.: Ueber anaphylaktische Organveränderungen bei Kaninchen, Virchows Arch. f. path. Anat. **289**:46, 1933.

those of other, nonrheumatic, vascular lesions of the brain. The consequences of the Nissl-Alzheimer type of meningoencephalic endarteritis are more complicated, however, than would be suspected from the study of sections stained with aniline dyes. I [61] have recently published a paper on the cerebral lesions of pernicious malaria studied with the silver impregnation technics of Río-Hortega; I observed that in malaria, as in other diseases producing vascular lesions of the brain, there arise alterations of the nerve fibers, of the true neuroglia, of oligodendroglia and, especially, of microglia which are of unsuspected extent and intense enough to explain the severe nervous symptoms of the patients. Even when the investigation of the central nervous system has been limited to use of aniline dyes investigators have noted some of these alterations in the brains of rheumatic patients. Such are the observations of Winkelman and Eckel,[62] whose paper on the subject is excellent, and Bodechtel,[40] Bruetsch [25] and Kernohan, Woltman and Barnes,[63] among the modern authors.

VASCULAR ALTERATIONS

The vascular lesions previously described involve the meningeal and cerebral arterioles and venules and appear especially in patients with chronic rheumatism. On the other hand, I found that all children, and a large number of adults who succumbed to acute rheumatic fever showed the capillary lesions to be described later. These capillary alterations appeared with maximal intensity and purity in those children who suffered from rheumatic encephalopathy during the last days of life, in the absence of severe heart failure or signs of secondary infection; in these cases the brain showed a characteristic "wet aspect" at autopsy.

According to the recent work of de Gortari, Pellón and Costero,[64] the salient feature of the clinical picture is the development of a state of mental stupor, which has a tendency to progress more or less rapidly toward coma. Frequently, this state is announced by prodromal signs or symptoms. During coma, profuse sweating and tonic or clonic

61. Costero, I., and Gómez Alanís, A.: Sobre las alteraciones encefálicas del paludismo pernicioso, Arch. histol. norm. y pat. **3**:227, 1946.

62. Winkelman, N. W., and Eckel, J. L.: Endarteritis of the Small Cortical Vessels in Severe Infections and Toxemias, Arch. Neurol. & Psychiat. **21**:863 (April) 1929; footnote 39.

63. Kernohan, J. W.; Woltman, H. W., and Barnes, A. R.: Involvement of the Nervous System Associated with Endocarditis, Arch. Neurol. & Psychiat. **42**:789 (Nov.) 1939.

64. de Gortari, A.; Pellón, R., and Costero, I.: Encefalopatía del reumático: I. Frecuencia insospechada de los accidentes cerebrales en el curso de la fiebre reumática y su papel como factores determinantes de la muerte, en 107 casos con el estudio correspondiente de necropsia, Arch. Inst. cardiol. México **17**:193, 1947; summary in Am. Heart J. **33**:716, 1947.

contractions are frequently observed, the latter affecting any part of the body. The stuporous state may be interrupted by periods of mental excitability, manifested as delirium, dysarthria, carphology or vomiting. Ordinarily, there is no increase of temperature or Cheyne-Stokes respiration. Frequently there is bradypnea; the pupils are dilated and their photomotor response is slow; the tongue is dry, the tendinous and musculocutaneous reflexes are slow and sometimes abolished; there is no incontinence, and the eye appears normal. This neurologic syndrome has been called encephalopathy of the rheumatic patient (de Gortari).

The macroscopic appearance of the brain in such cases is characteristic. Even the smallest vessels in the brain, as well as those in the meninges, are full of blood; when the knife is passed over the surface of the section, many of the vessels do not disappear, because the blood is not in the lumen but in the Virchow-Robin space. In the white substance of the brain, in the basal ganglia and sometimes in the entire central nervous system, there are hemorrhagic points. In addition, the neural parenchyma is tense, hard and elastic; it shows a brilliance similar to that of genuine edema, and on its external surface there are signs of pressure against the bony structures of the skull, as in acute traumatic tumefaction. The sum of these macroscopic features constitutes the wet brain described by Costero and associates.[64]

When such a brain is stained by aniline dyes, the lesions observed are those described by Winkelman and Eckel[39] and by many others. One has the impression that there has been little reaction to the punctiform hemorrhages and that the vascular alterations are scarce and of moderate intensity, and only a few small acellular areas can be discovered.

The picture is entirely different when these sections are stained for precollagen fibers. In this case, profound alterations are seen in the vast majority of the vessels, especially in the capillaries. On one hand, there is intense dilatation of the perivascular lymphatic space of Virchow and Robin; on the other, there is a variable degree of sclerosis due to newly formed argyrophilic precollagenous fibrils. Both these phenomena, the dilatation of the lymphatic space and the sclerosis, seem to maintain an intimate relation (Costero, Barroso-Moguel, de Gortari and Pellón[65]).

The dilatation of the lymphatic space can be recognized regardless of the staining method used, so long as the sections have been cut on the freezing microtome; the perivascular dilatation is not an artifact, since both normal and altered vessels are seen in the same section (figs. 1 and *2*, *1* to *10*). However, *1* and *2* of figure 1 are especially demonstrative of this change, because the nerve fibers are intensely

65. Costero, I.; Barroso-Moguel, R.; de Gortari, A., and Pellón, R.; Encefalopatía del reumático: II. Cuadro histopatológico del encéfalo jugoso, Arch. Inst. cardiol. México **17**:488, 1947.

impregnated whereas the unstained lymphatic space is clearly outlined. In *1* (fig. 1) an arteriole from a superficial layer of the cortex is shown, without evident alterations of its wall. In *2* there is a venule of somewhat deeper situation, with slight irregularities in the disposition and staining of the endothelium. In some places its dilated lymphatic space is filled with blood, so that the clearness of observation is increased (fig. 1, *3*).

The sclerosis is always diffuse and frequently involves the majority of the cerebral vessels, as in *4* of figure 1, in which a group of capillaries of the white matter is reproduced; the walls of the unaltered vessels appear as continuous endothelial tubes, moderately and uniformly argyrophilic, while the sclerotic vessels present a filamentous appearance of various degrees of complexity. Similar lesions can be observed in any other part of the brain, such as the pons Varolii (fig. 1, *5*).

The morphologic process of capillary fibrosis develops in three successive stages. In the first stage, the argyrophilic fibers are limited to isolated patches, almost always near a point of division of the vessel (fig. 2, *6*); a dense reticulum, consisting of fine filaments, is formed. The second period is characterized by loosening of the argyrophilic fibrils, which acquire a certain degree of autonomy (fig. 2, *7*); soon they become larger and reach the neighboring vessels (fig. 2, *8*), and finally they completely cover them (fig. 2, *9*). In the last stage, the altered vessels appear surrounded by a thick network of swollen fibers with a few anastomoses of a predominantly longitudinal course and with a conspicuous tendency toward collagenous transformation (fig. 2, *10*).

The dilatation of the lymphatic perivascular space must be related to an increase in the permeability of the capillary endothelium (Kubie[66]). In my sections, and with the use of Río-Hortega's technics, I have been unable to find morphologic alterations in the endothelium which could be related to an increase of its permeability. Only in some places does the vascular wall appear irregularly thickened (fig. 1, *2*), as though some of its cells were swollen; in other places, argyrophilic granulations of unknown significance are observed. The lymphatic spaces are usually dilated in areas of the brain showing intense congestion; however, in some cases I have seen intense dilatation of these spaces when the congestion was not conspicuous. It is probable, therefore, that the vascular congestion is not the only factor responsible for the increase of capillary permeability.

On the other hand, capillary sclerosis always begins in those places in which the lymphatic perivascular space is dilated, especially where

66. Kubie, L. S.: Changes in Intracranial Pressure During Forced Drainage of the Central Nervous System: The Hydratation Factor, Brain **51**:244, 1928; Intracranial Pressure Changes During Forced Drainage of the Central Nervous System, Arch. Neurol. & Psychiat. **16**:319 (Sept.) 1926.

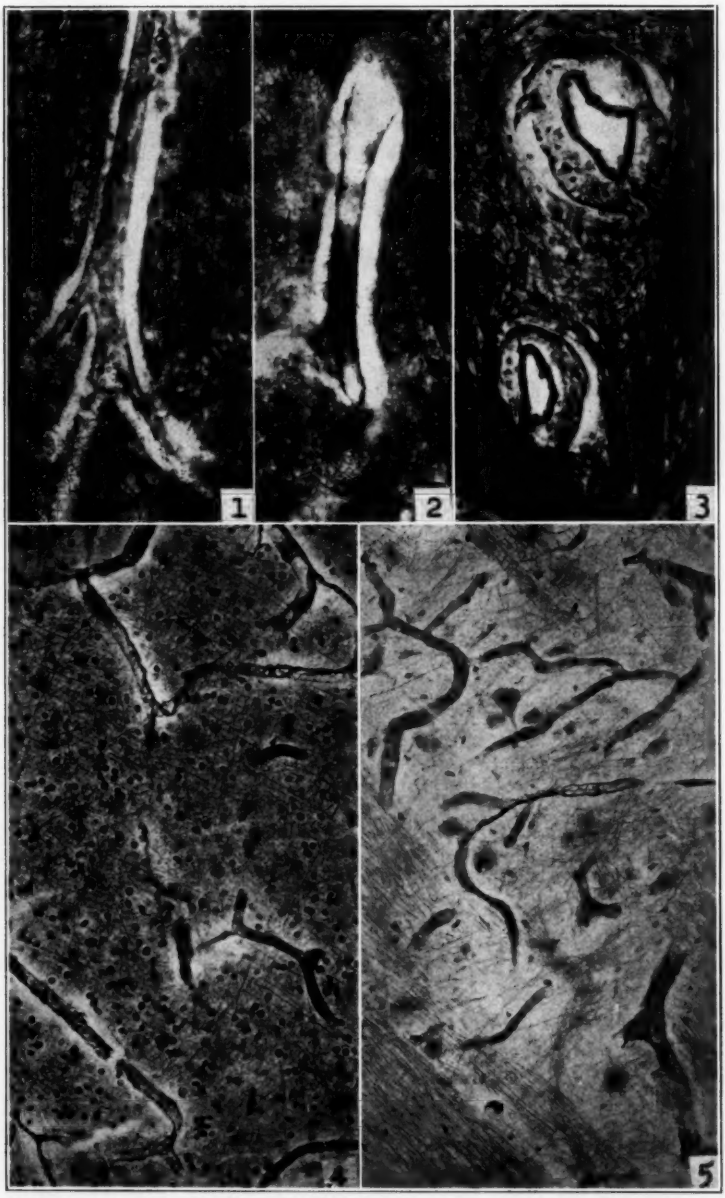

Fig. 1.—*1*, dilatation of the lymphatic space in an arteriole from a superficial layer of the cerebral cortex; *2*, dilatation of the lymphatic space in a venule, with slight irregularities in the disposition and staining of the endothelium; *3*, dilatation of the lymphatic space occupied by blood in a cerebral arteriole; *4*, group of sclerotic capillaries of the white matter of the brains in a case of rheumatic fever; *5*, capillary sclerosis in the pons Varolii. × 165.

there is an increased number of perivascular histiocytes, that is, at the points of branching. These circumstances, which are in accordance with others observed by me [67] under different pathologic conditions, in a variety of sites in the body, have led me to conclude that the argyrophilic fibrils are formed from the adventitial histiocytes. These cells behave as true fibroblasts when irritated by hematogenous substances, probably fibrinogen or similar compounds.

HEMORRHAGES

The increase in the permeability of the cerebral capillaries during the attacks of rheumatic fever manifests itself in various ways. Clinically, one finds many of the symptoms already described. At autopsy the wet aspect of the brain is striking, due largely to the genuine edema. Microscopically, there are not only dilatations of the pericapillary lymphatic spaces, but also numerous hemorrhages, produced by diapedesis, which are difficult to see grossly. The red blood cells pass into the dilated lymphatic space and circulate through it until they surround the great vascular trunks (fig. 1, *3*); these trunks may be compressed by the dense coat of blood cells surrounding them. In general, diapedetic hemorrhages are not followed by conspicuous alterations of the nerve structures; when they are sufficiently intense, they may be recognized on simple inspection, because, even after the surface of the cut is cleaned with the knife blade, the vascular pattern persists.

In the wet brain, hemorrhages by diabrosis are never lacking; such hemorrhages are almost always of the annular type and are often so abundant that they constitute a well defined picture of cerebral purpura. These hemorrhages are localized most commonly in the white matter of the brain, the basal ganglia and the pons Varolii. When the hemorrhage is recent, the capillary is found in the center, profoundly altered and surrounded by a halo of necrobiosis (fig. 3, *11*); the red blood cells infiltrate regularly the neighboring nerve tissue, producing characteristic alterations in it. In the first stages, the nerve fibers placed close to the infiltration become separated, stain intensely with silver and form a typical reticular sponginess. Later, the axis-cylinders are sectioned at the level of the necrobiosis and develop buds of regeneration, as in figure 3, *12*. The regeneration may be frustrated, and in such a case retraction spheres are found during a long period, next to the hemorrhagic vessels; ordinarily, however, the axis-cylinders continue to grow and establish aberrant fibers; when these fibers cross each other irregularly, they show a structure similar to a small amputation neuroma (fig. 3, *13*), made up of distorted fibers devoid of myelin sheath.

67. Costero, I.: Significado de la linfocitosis intersticial en el reumatismo y en otros procesos inflamatorios, con una interpretación global de las principales lesiones reumáticas, Arch. Inst. cardiol. México **16**:471. 1946; abstracted in Am. Heart J. **33**:717, 1947.

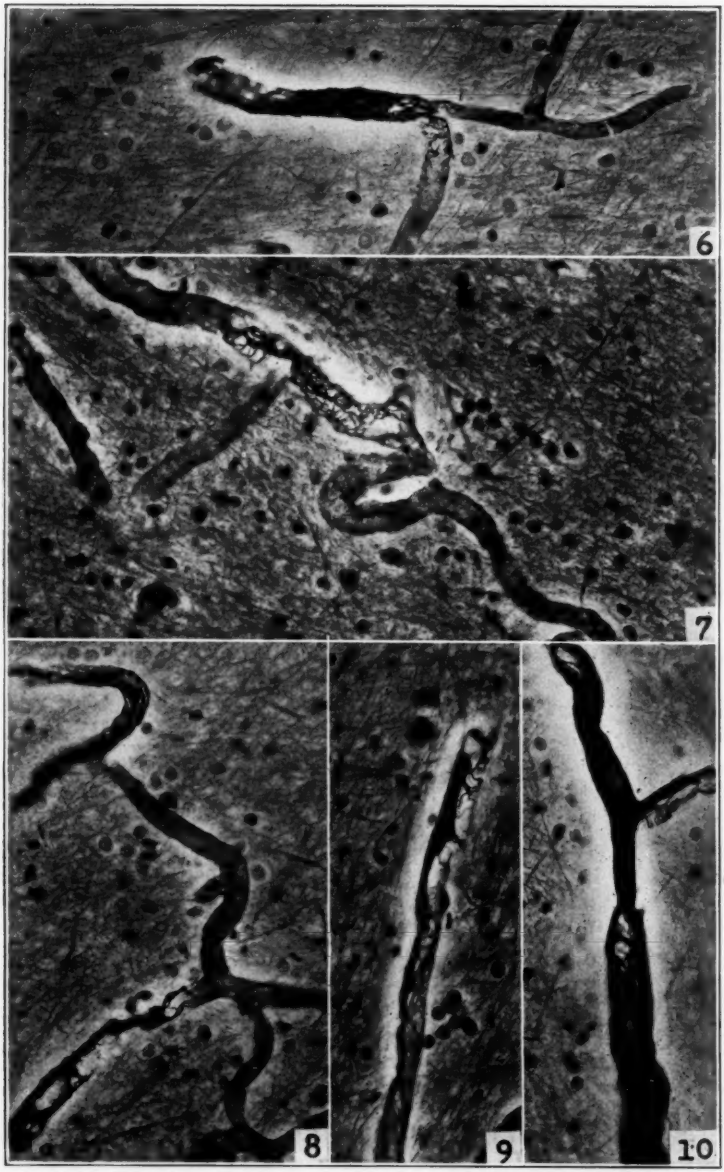

Fig. 2.—*6*, first phase of capillary sclerosis. The argyrophilic fibers are limited to isolated sites, in places where the lymphatic spaces are dilated. *7-9*, second phase of capillary sclerosis. The argyrophilic fibers are loosened and acquire a certain degree of autonomy (*7*). The fibers become larger and reach the neighboring vessels (*8*). The argyrophilic fibers completely cover the vessel (*9*). *10*, third phase of capillary sclerosis. The altered vessels appear surrounded by a thick network of swollen fibers with a decided tendency toward collagenous transformation. × 330.

The true neuroglia is not always affected. It is only in the vicinity of a few fresh hemorrhages that some fibrous astrocytes of great size can be discovered; these hypertrophied elements persist even after the red cells have disappeared and are similar to the cells surrounding vessels with diapedetic hemorrhages.

In all pathologic processes of the brain, as discovered by del Río-Hortega,[68] the microglia has the function of absorbing the extravasated red blood cells, as well as the necrotic tissue. Microglia also plays this role in the hemorrhages of rheumatic patients; enormous quantities of Hortega cells accumulate among the extravasated red cells, assuming pseudopodic forms similar to those of the ordinary macrophages of connective tissue. All their branching processes disappear, while an accumulation of fat droplets in the cytoplasm gives it a reticular aspect; the greater part of the cells are transformed into compound granular cells, which phagocytose red blood cells. Specific staining for microglia reveals that the freshest hemorrhages are free from mobilized Hortega cells. After from two to six days of evolution, some mobilized Hortega cells are seen in the periphery of the lesion, moving toward the extravasated blood cells. After about two weeks, the entire hemorrhagic zone is invaded by compound granular cells; the central vessel, the necrobiotic halo and many red blood cells phagocytosed by the microglia cells may still be distinguished (fig. 3, 14). Owing to the function of phagocytosis performed by the microglia, the red blood cells of the lesions gradually disappear, while the compound granular cells become separated by a slow migration toward the periphery. Later, there are only a few scattered compound granular cells close to the débris of the initially necrotic zone. Thus, of the oldest hemorrhages nothing remains but well limited accumulations of compound granular cells. Such microglial nodules have been found in some cases of rheumatism by Winkelman and Eckel [39] and by Bruetsch [25]; they are similar in structure and significance to those described by Winkelman and Eckel,[62] Spielmeyer,[69] Globus,[70] Scholz [71] and Costero y Gómez Alanís [61] in hemorrhagic diseases of the brain other than rheumatism.

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68. del Río-Hortega, P.: La microglía y su transformación en células en bastoncito y en cuerpos granuloadiposos, Trav. du lab. Inv. biol. de l'Univ. de Madrid **10**:1, 1919; Poder fagocitario y movilidad de la microglía, Bol. Soc. españ. de biol. **9**:154, 1919; Histogénesis y evolución normal de la microglia, Mem. r. Soc. españ. hist. nat. **11**:213, 1921.

69. Spielmeyer, W.: Infektion und Nervensystem, Ztschr. f. d. ges. Neurol. u. Psychiat. **123**:161, 1930.

70. Globus, J. H.: Inflammatory Disease of the Central Nervous System: So-Called Nonsuppurative Encephalitis and Encephalomyelitis, Arch. Neurol. & Psychiat. **28**:810 (Oct.) 1932.

71. Scholz, W.: Herdförmige protoplasmische Gliawucherungen von syncytialem Charakter; Ausblick auf Bedeutug für den Verlauf des pathologisch-anatomischen Prozesses bei der Encephalitis epidemica, Ztschr. f. d. ges. Neurol. u. Psychiat. **79**:114, 1932.

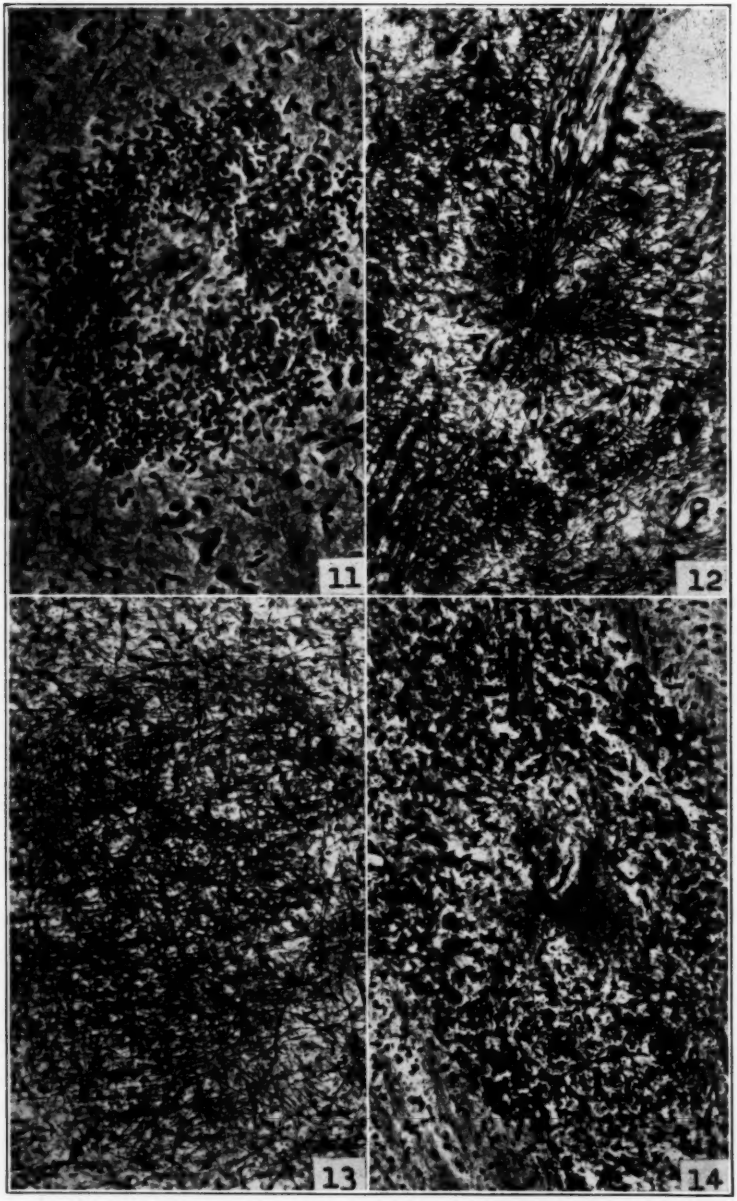

Fig. 3.—*11*, fresh annular hemorrhage with an altered capillary in the center, a halo of necrobiosis and extravasated red blood corpuscles; × 165. *12*, axis-cylinders sectioned at the level of the necrobiosis, with buds of regeneration; × 165. *13*, aberrant nerve fibers crossing each other irregularly, the structure resembling that of a small amputation neuroma. × 165. *14*, annular hemorrhage invaded by compound granular cells (ameboid microglia); × 82.5.

The consequences of the cerebral hemorrhages must be severer for the patient than could be deduced exclusively from the morphologic analysis of the lesions described. As we have already stated, the brain of a patient with active rheumatic fever shows not only genuine edema but also signs of acute tumefaction, such as are found frequently after surgical or accidental trauma to the skull. The acute swelling of the rheumatic brain is not so intense as that elicited by mechanical means, and has many features in common with those of hemorrhagic encephalitis and nonrheumatic cerebral purpura. It seems likely that the acute swelling, and not the edema, is responsible for the coma preceding death in such cases, since the cerebral edema maintains itself for at least several weeks, until it gives rise to capillary sclerosis, whereas the coma lasts only a few hours. Acute swelling seems to be initiated by the hemorrhages; these, in turn, are due to the lesions of the endothelium, which when they are slight, increase the permeability of the capillaries.

AREAS OF DEVASTATION (ACELLULAR AREAS)

Since the work of Nissl and of Alzheimer, it has been generally accepted that proliferative endarteritis of meningoencephalic vessels leads commonly to development of the so-called acellular areas of the cerebral cortex. From the study of my material, one may infer that at least in rheumatism many if not all of the acellular areas represent a permanent residuum of old hemorrhages produced during the acute period of the disease and that these areas are by no means as poor in cellular elements as has been thought from sections stained with aniline dyes. I have come to this conclusion after studying abundant material collected in cases of recurring attacks of severe rheumatic fever; this material has been stained with del Río-Hortega's technic for microglia and for neuroglia.

In the wet brain it is difficult to find an extensive zone containing an entirely normal microglia. The majority of Hortega cells have few prolongations and have lost the greater part of their characteristic spinous processes; the perinuclear cytoplasm is abundant and spongy and in contour shows a large number of prominences. Many cells are adherent to the capillaries, and in this position they often lose their prolongations, or at least their secondary ramifications. This stage of diffuse mobilization of the microglia is of basic significance in evaluating the importance of the general metabolic alterations of the nerve tissue and indicates that the vascular lesions are more intense than has usually been thought and that they have consequences of greater significance than would be suspected by studying the brain with stains of low specificity.

During the acute attack of rheumatic fever the mobilization of the microglia reaches an extraordinary intensity in some places. Figure 4, *15* shows a wide zone of the cerebral cortex filled with rod cells; this zone is comparable only to that seen in cases of dementia paralytica.

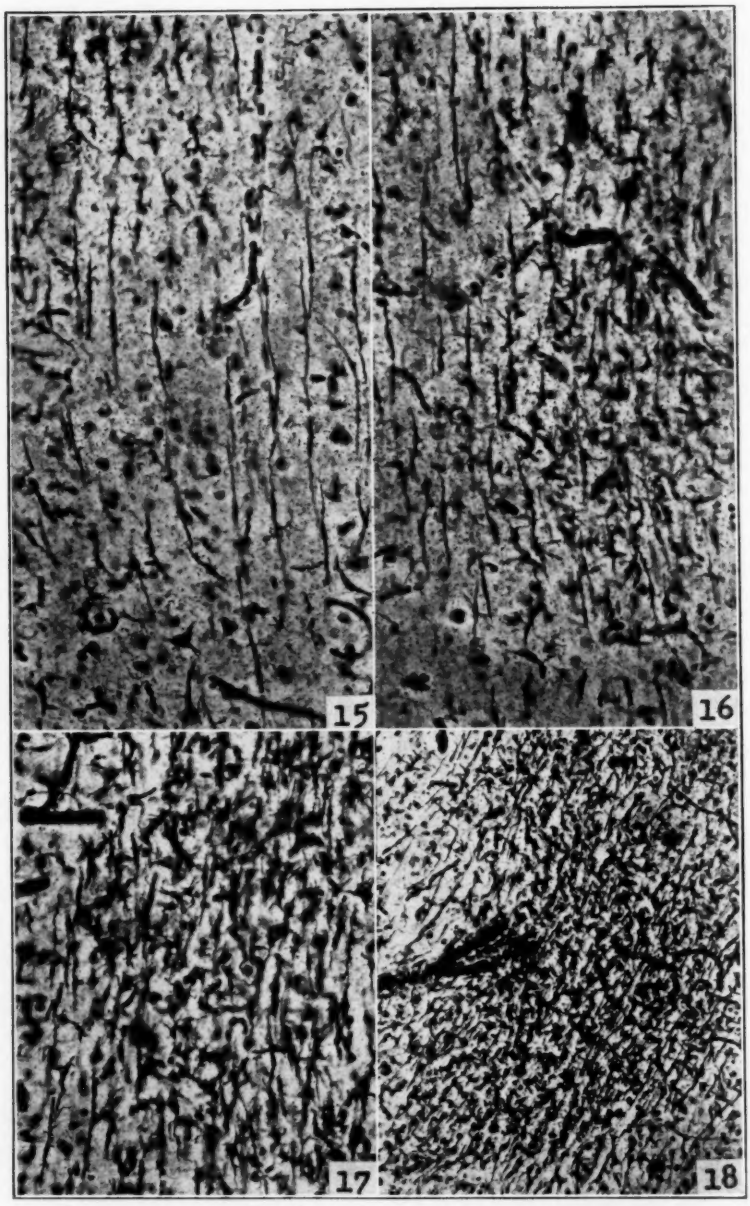

Fig. 4.—*15*, wide zone of the cerebral cortex filled with rod cells, a picture corresponding to that called *Stäbchenzellenencephalitis;* × 165. *16*, another zone with intensely mobilized microglia, forming dense areas of diffuse infiltration; × 165. *17*, area of devastation (acellular area), with abnormal aspect of one of the regional vessels and absence of compound granular cells; × 165. *18*, areas of devastation, with microglial infiltration more clearly outlined and with more conspicuous vascular abnormalities; × 82.5.

The patient was a child with clinical symptoms of acute and severe rheumatic encephalopathy, without any sign of syphilis or of superimposed infection; nevertheless, the picture corresponds to what has been called *Stäbchenzellenencephalitis* by Kernohan, Woltman and Barnes.[63]

Another zone with intensely mobilized microglia cells, forming dense areas of diffuse infiltration, is reproduced in figure 4, *16*; rod cells and pseudopodal elements are profusely intermingled, in spite of the fact that there were no significant alterations of the nerve cells in this area, nor were there necrotic or hemorrhagic zones.

Figure 4, *17*, shows an area of devastation, wrongly called an acellular area. The abnormal aspect of one of the regional vessels, to be precise, the one placed within the accumulation of mobilized microglia, is apparent, as well as the absence of compound granular cells and the relatively sharp limitation of the infiltrative foci. The limit of the infiltration is still more clearly outlined, and the vascular abnormalities are more conspicuous in the area of devastation shown in figure 4, *18*.

These dense groups of Hortega cells constitute the chief, but not the only, structure in the areas of devastation. In *19* of figure 5 it is possible to observe the presence of fibrous neuroglial elements, with slightly ramifying prolongations, arranged in the form of a focus of gliosis; this picture is repeated without great variation in all the areas of devastation of cerebral cortex. In other parts of the brain, especially in the basal ganglia and in the brain stem, the areas of devastation are not so clearly visible, and in order to disclose them it is necessary to have highly specific stains for microglia. On the other hand, the proliferation of the local vessels and the connective tissue sclerosis are more intense in these areas than in the cerebral cortex; this facilitates the identification of areas of devastation by the use of technics for reticular fibers, giving pictures similar to that in figure 5, *20*. The connective scar constitutes a network of irregular threads, anchored in many sclerotic capillaries.

In view of the alterations of the microglia that I have just described, the term "nonsuppurative meningoencephalitis" given by Winkelman and Eckel[39] to rheumatic encephalopathy seems justified. However, even though the clinical and morphologic data now available support the existence of an inflammatory process in the brain during the evolution of rheumatic fever, it seems desirable to accept the modern opinion on the evaluation of inflammatory processes which has prevailed among pathologists for the last decades, namely, that aside from genuine inflammation, there exist a reparative inflammation and a physiologic inflammation. One would agree that the lesions of the brain in rheumatic fever have their place among the reparative inflammations. This is why de Gortari, Pellón and I[64] did not use the term encephalitis but preferred that of encephalopathy for the changes in the brain of rheumatic patients; the majority of neurologists prefer to limit the term encephalitis to its strict sense (Globus[70]).

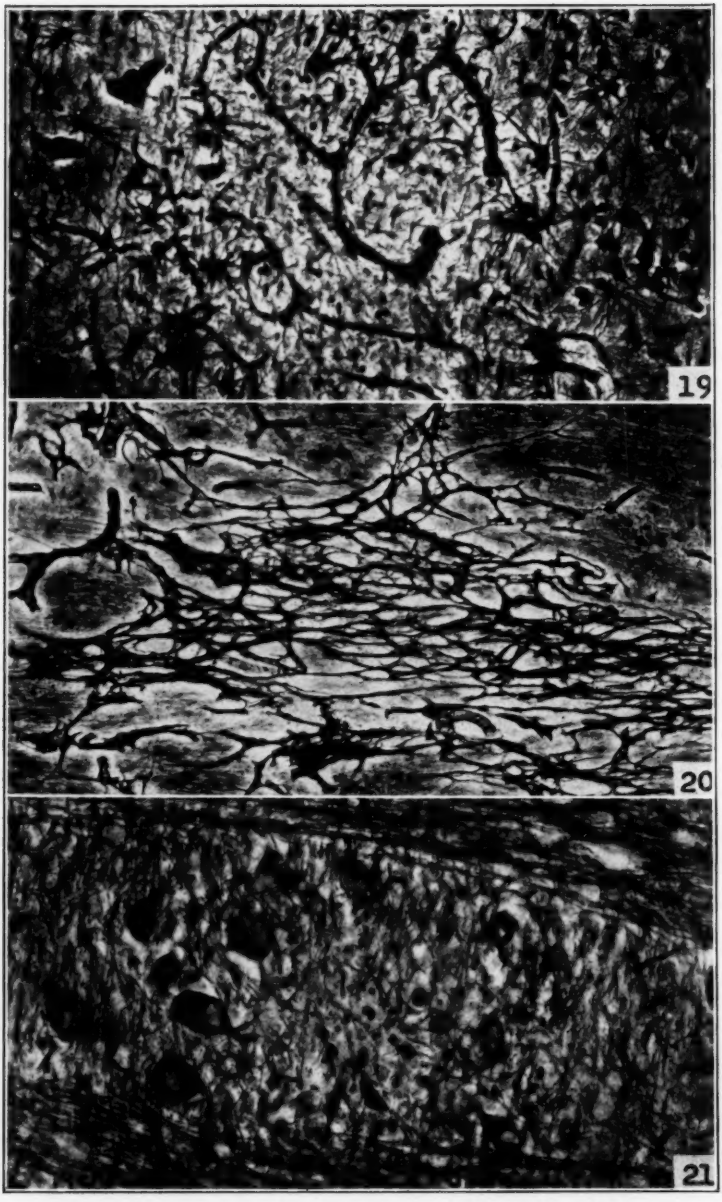

Fig. 5.—*19,* fibrous neuroglial cells, with slightly branching prolongation, arranged in the form of a focus of gliosis, in an area of devastation of the cerebral cortex; × 330. *20,* connective tissue scar forming a network of irregular threads, anchored to many sclerotic capillaries. This scar corresponds to an area of devastation found in the pons Varolii; × 165. *21,* small foci of neuronal destruction observed only when the nerve fibers are correctly stained. Miliary necrobiosis of this type is the beginning of the nodules of branching microglia cells; × 330.

FOCI OF SOFTENING

This study would be incomplete without the consideration, briefly, of the foci of softening in the brain which are frequently associated with rheumatic disease. It is generally agreed that these foci represent a complication due to extensive hemorrhage, local thrombosis or embolism. When secondary bacterial endocarditis supervenes, the embolism may be accompanied with septic phenomena in the brain.

In any case, the foci of softening do not present any special feature. The zones of destruction show characteristic signs of degeneration and are soon invaded by compound granular cells; furthermore, in the perivascular lymphatic spaces there appear lipid substances, which stain with scarlet red, and wandering compound granular cells. At the beginning the ameboid neuroglia cells of Nissl can be seen within the limits of the lesion, and later there are plaques of gliosis, generally dense and fibrous. The connective tissue of the great vascular trunks proliferates, until sometimes a collagenous scar is formed; this complication is ordinarily not extensive in cases of rheumatic fever.

SPECIFICITY OF THE LESIONS

It is generally accepted that none of the phenomena described hitherto—alterations of the small cerebral vessels, hemorrhages, areas of devastation and foci of softening—is sufficiently specific to be used as unequivocal evidence for the diagnosis of rheumatic fever. It should be added that these cerebral lesions, considered as a whole, constitute a morphologic picture which is never absent during the evolutive phase of rheumatic fever, and that they are more dangerous to the life of the patient than the circulatory insufficiency. Thus, the 32 children of my series and the 50 of the 75 adults studied have died as an immediate consequence of the cerebral lesions, after a clinical picture of encephalopathy refractory to all types of treatment.

Nor can I say that the sclerosis which I have described in the cerebral capillaries is due exclusively to rheumatic fever; however, it is more intense and extensive in rheumatism than in any other pathologic process. It must be taken into account that capillary sclerosis is probably a concomitant phenomenon of chronic cerebral edema and that patients with intoxications or infectious diseases usually die shortly after the onset of cerebral edema. In any case, I believe that telangiosclerosis of the brain can be considered only as one more feature of the pathology of rheumatism.

In addition to all the lesions which have occupied our attention, there are others which I have not found described in the literature, and which may serve as an important basis for establishing the specificity of rheumatic encephalopathy. These lesions are certain nodules of branching microglia, different from those heretofore described in any

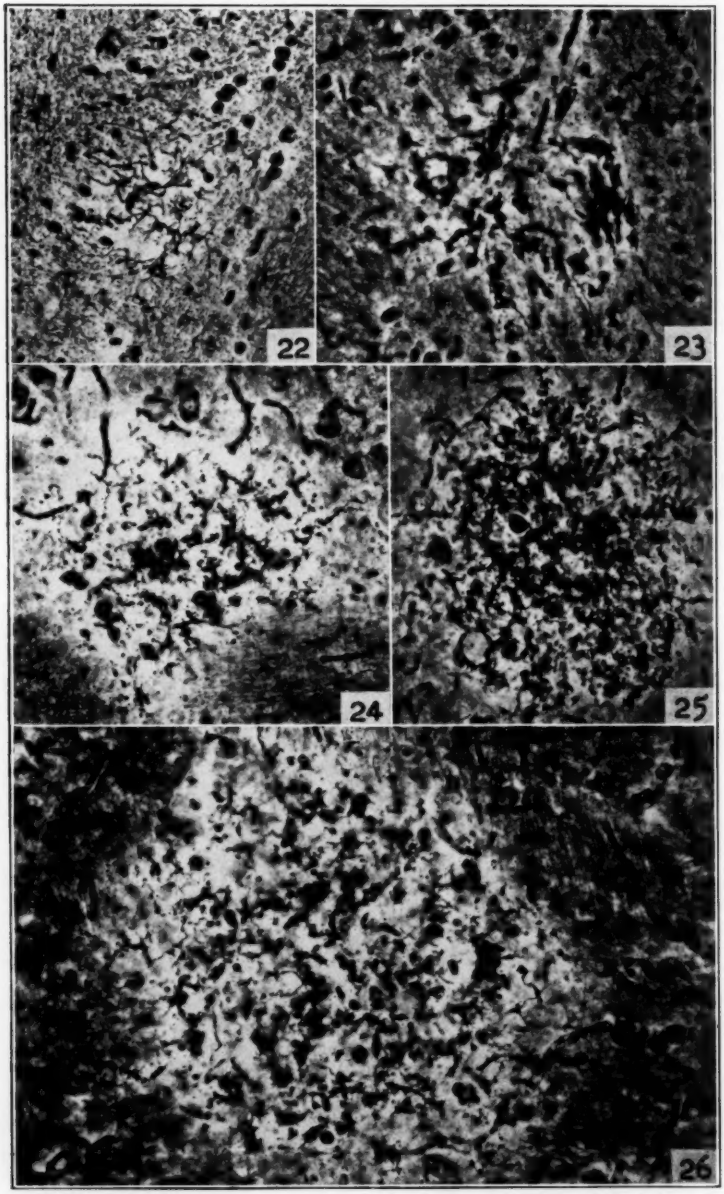

Fig. 6.—*22,* small microglial nodule formed by the confluence of a few Hortega cells; *23,* another fresh microglial nodule situated near a blood vessel; *24,* typical nodule of branching microglia cells, with the prolongations of the Hortega cells broken down into small, irregular lumps, connected by fine filaments, on which they appear threaded in the manner of a rosary; *25,* another typical nodule of branching microglia cells, with clasmatodendrosis and large, ovoid cells, corresponding to protoplasmic neuroglia cells, placed within the nodule; *26,* portion of nerve tissue surrounding the nodule stained weakly with silver carbonate, due to demyelination. × 165.

other pathologic process, with characteristic morphology and apparently independent of the vascular lesions, the hemorrhages, the areas of devastatión and the softening foci.

These nodules are neither frequent nor easy to discover. Apparently, they constitute a passing phenomenon, present only in the brain of patients with active rheumatic fever and limited to a short period after first recurrence, between the fourth and the eighth week. I have found them more abundantly in the brain stem, especially in the pons Varolii. In the most favorable cases, many transverse sections do not contain any nodules, and in other sections there may be as many as six, as a result of their irregular distribution. The number of nodules seems to be independent of the extent and intensity of other cerebral lesions. The patients who showed nodules of branching microglia in the brain also had fine, fresh fibrinous granulations, similar to drops of dew, in the heart valves. To date I have found such foci of branching microglia cells in only 6 cases, all of children. In view of this small number of cases, it is understandable that these observations are subject to possible correction.

The nodules of branching microglia seem to appear first in miliary areas of necrobiosis, which most frequently are not situated close to a vessel. The necrobiosis seems to involve, above all, the thick prolongations of the nerve cells, which are fragmented and deformed in limited areas of the brain. In order to discover these small foci of neuronal destruction, it is necessary to study sections correctly stained for nerve fibers, and to observe them thoroughly. Figure 5, *21* is a good illustration of the aspect of this lesion.

However, it is with Río-Hortega's method for microglia that I have been able to recognize the principal morphologic characteristics of these nodules. All are of small size; the smallest are formed by the confluence of a dozen Hortega cells, with complex crossings of their prolongations (fig. 6, *22*); the largest do not exceed a diameter of 500 microns (fig. 6, *26,* and fig. 7, *27* and *30*); most commonly they are regularly rounded and have an average diameter of 250 microns (fig. 6, *25* and fig. 7, *28* and *29*).

Irrespective of their situation and size, the nodules are formed by branching Hortega cells with clasmatodendrosis, i. e., with fragmentation of their prolongations into small, irregular lumps, almost always rounded or piriform and intensely argyrophilic. Many of the lumps arising from the breaking down of the microglial prolongations become connected by fine filaments, on which they appear threaded, in the manner of a rosary (figs. 6 and 7, *24* to *30*). These cells stain more easily than do normal microglia cells so that it is possible to obtain preparations in which the nodular microglia is stained intensely in an almost selective manner. I have never observed microglia with polymorphous or multiple nuclei.

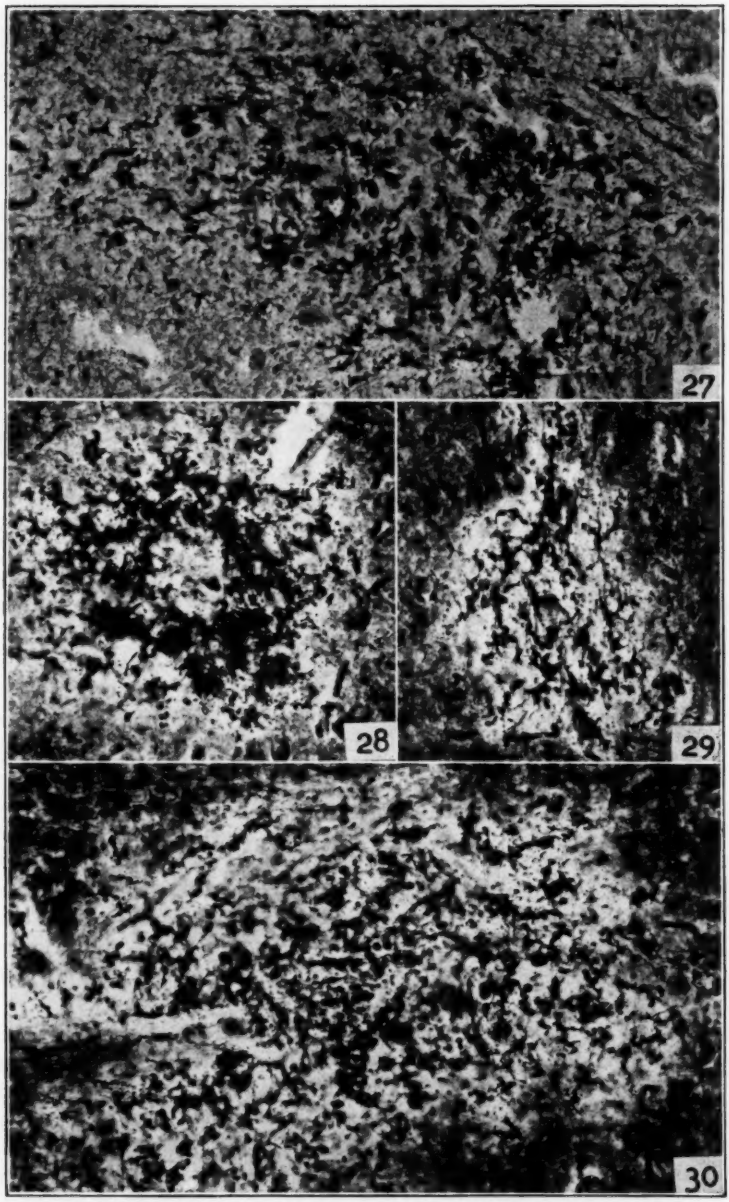

Fig. 7.—*27*, large nodule situated in the vicinity of a blood vessel, establishing a tangential contact. *28*, microglial nodule surrounding an altered blood vessel. No extravasated red blood corpuscles are seen. *29*, a few extravasated red blood cells between the microglial cells of the nodule. These erythrocytes seem to have been recently extravasated, because they are not phagocytosed by the microglia. *30*, microglial nodule surrounding a capillary with a fresh hemorrhage, probably due to the development of the lesion. × 165.

The part of the nerve tissue surrounding each nodule almost always stains weakly in silver preparations because it has lost its myelin, so that round or ovoid, large cellular nuclei appear sharply outlined in it (figs. 6 and 7, *24* to *30*); these nuclei belong to neuroglia cells of the protoplasmic variety, or at least to glia cells with highly branched and spongy prolongations. In contrast to the sequence of events in the areas of devastation, which are generally invaded by newly formed capillaries and networks of reticular fibers because of their scarlike character, the neighboring capillaries do not penetrate the foci of branching microglia cells, and these foci behave as ischemic zones as compared with the unaltered limiting tissue.

The nodules may be seen surrounding blood vessels (fig. 6, *23*; fig. 7, *30*), and it is then sometimes possible to discover a few extravasated red blood corpuscles between the microglia cells. In other cases the nodules may be situated next a vessel, establishing a tangential contact (fig. 7, *27*). However, the great majority of the nodules are independent of the vessels and lie in the gray matter. Whenever nodules of branching microglia cells are observed close to blood vessels, one has the impression that these vessels have been accidentally included in the nodular lesion, and have become obstructed and devoid of circulation. Although it is difficult to judge the significance of the extravasated blood cells which sometimes are found among the microglia cells of the paravascular nodules, I feel that they are more likely to represent a secondary hemorrhage in consequence of the lesions produced in the vessel by the vicinity of the nodule, than to consist of the residuum of an old hemorrhage which has initiated the nodular lesion.

I am unable at this moment to establish the exact meaning of the nodules of branching microglia. I had the good fortune of working for fourteen consecutive years next to the working bench of the man who discovered microglia, Dr. Pío del Río-Hortega, the investigating genius to whom we owe the sum of our actual knowledge regarding the morphology, the origin and the functional activity of this third element in the central nervous system; from this teacher I learned to question the specific character of the pathologic reactions of microglia. However, my own experience with these pathologic reactions is ample enough, and this is the first time that I have found such nodules, and only during this study of the brains of rheumatic patients.

Doubtless it is dangerous to base the specificity of the nodules of ramifying microglia on such negative arguments as I have presented. However, it seems to me probable that these nodules will be proved to be due to a hyperergic response, comparable in the nervous system to the process represented by the Aschoff nodule in the connective tissue. It is possible, therefore, that the nodules of ramifying microglia represent

a specific lesion, of comparable diagnostic value to that of the encephalic nodules described by Fränkel [72] and Spielmeyer [73] for exanthematic typhus, by Schröder [74] for pernicious anemia, by Dürck [75] for pernicious malaria, by Hassin [76] for poliomyelitis and by Stern [77] and Scholtz [71] for epidemic encephalitis.

I am aware of the objections which could be made to this supposition, but I cannot consider it as devoid of foundation. First, the microglia is undoubtedly a mesodermic element in the brain with biologic properties similar to those of the histiocyte of connective tissue (del Río-Hortega,[78] Globus,[79] Metz and Spatz,[80] Alberca,[81] Gallego,[82] Creutzfeld and Metz,[83] Spatz,[84] del Río-Hortega and Penfield,[85] Penfield,[86]

72. Fränkel, E.: Ueber das Verhalten des Gehirns bei akuten Infectionskrankheiten, Virchows Arch. f. path. Anat. **194**:168, 1908.

73. Spielmeyer, W.: Die zentralen Veränderungen beim Fleckfieber und ihre Bedeutung für die Histopathologie der Hirnrinde, Ztschr. f. d. ges. Neurol. u. Psychiat. **47**:1, 1919.

74. Schröder, P.: Grosshirnveränderungen bei perniziöser Anämie, Monatschr. f. Psychiat. u. Neurol. **35**:543, 1914.

75. Dürck, H.: Ueber die bei Malaria perniciosa comatosa auftretenden Veränderungen des zentralen Nervensystems, Arch. f. Schiffs- u. Tropen Hyg. **21**:117, 1917.

76. Hassin, G. B.: Brain Changes in Typhus Fever Contrasted with Those in Epidemic Encephalitis and Acute Poliomyelitis, Arch. Neurol. & Psychiat. **11**:121 (Feb.) 1924.

77. Stern, F.: Die epidemische Encephalitis, Berlin, Julius Springer, 1928.

78. del Río-Hortega, P.: Concepts histogénique, morphologique, physiologique et physio-pathologique de la microglie: Rev. Neurl, **1**:956 (June) 1930. Microglia, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932.

79. Globus, J. H.: Glia Response in Chronic Vascular Disease of the Brain, Arch. Neurol. & Psychiat. **20**:14 (July) 1928.

80. Metz, A., and Spatz, H.: Die Hortegaschen Zellen (das sogenannte "dritte Element") und über ihre funktionelle Bedeutung, Ztschr. f. d. ges. Neurol. u. Psychiat. **89**:138, 1924.

81. Alberca, R.: Intrevención precoz de la microglía en las heridas experimentales de la medula espinal, Bol. Soc. españ. de biol. **11**:81, 1926.

82. Gallego, A.: Alteraciones vasculares y de la microglía en el moquillo del perro, Bol. Soc. españ. de biol. **12**:32, 1926.

83. Creutzfeld, H. G., and Metz, A.: Die morphologische und funktionelle Differenzierung der Neuroglia, Zentralbl. f. d. ges. Neurol. u. Psychiat. **33**:445, 1923; Ueber Gestalt und Tätigkeit der Hortegazellen bei pathologischen Vorgängen, Ztschr. f. d. ges. Neurol. u. Psychiat. **106**:18, 1926.

84. Spatz, H.: Untersuchungen über Stoffspeicherung and Stofftransport im Nervensystem, Ztschr. f. d. ges. Neurol. u. Psychiat. **100**:428, 1926.

85. del Río-Hortega, P., and Penfield, W.: Cerebral Cicatrix, Bull. Johns Hopkins Hosp. **41**:278, 1927.

86. Penfield, W.: Phagocytic Activity of Microglia in the Central Nervous System, Proc. New York Path. Soc. **25**:71, 1925.

Schaffer,[87] Jiménez de Asúa,[88] Spielmeyer,[89] Costero [90]); it is well known that from the histiocytes during hyperergic reactions specific granulomas are formed, among them the Aschoff nodule. Second, we cannot expect the hyperergic reactions in the brain to begin by fibrinoid necrosis, since this special form of allergic necrosis is intimately connected with the precollagenous network of the connective tissue (Costero [91]), and in normal nerve tissue this structure is practically absent. Finally, in my present experience the nodules of ramifying microglia appear in those patients in whom Aschoff nodules are present in other parts of the body. I hope that more light may soon be thrown on this important problem.

CONCLUSIONS

1. During the developmental periods of rheumatic fever the capillary vessels are always profoundly altered throughout the brain. The alterations consist in (*a*) dilatation of the lymphatic perivascular space; (*b*) neoformation of argyrophilic precollagen fibrils from the perivascular histocytes; (*c*) growth of these fibrils, resulting in the formation of a reticular coating which surrounds long segments of the capillaries, and (*d*) collagenous transformation and hyalinization of the reticulum, with production of capillary sclerosis.

2. The dilatation of the lymphatic space corresponds to an increase in the permeability of the capillary endothelium, such as is found in true cerebral edema. The passage of blood proteins causes irritation of the perivascular histiocytes, stimulating them to fibroblastic activity and giving rise to the sclerosis.

3. The cerebral hemorrhages of patients with active rheumatic fever are related to the increase of permeability of the capillaries. Most frequently they are produced by diapedesis, and in this case the blood passes into the dilated lymphatic spaces without provoking a morpho-

87. Schaffer, K.: Ueber die Hortegasche Mikroglia, Ztschr. f. d. ges. Anat. **81**:715, 1926.

88. Jiménez de Asúa, F.: Die Mikroglia (Hortegasche Zellen) und das retikuloendotheliale System, Ztschr. f. d. ges. Neurol. u. Psychiat. **59**:354, 1927.

89. Spielmeyer, W.: Histopathologie des Nervensystems, Berlin, Julius Springer, 1922.

90. Costero, I.: Cultivo "in vitro" de microglía, Bol. r. Soc. españ. de hist. nat. **30**:165, 1930; Studien an Mikrogliazellen (sog. Hortegazellen) in Gewebskulturen von Gehirn, Arb. a. d. Staats-Inst. f. exper. Therap. **23**:27, 1930; Estudio del comportamiento de la microglia cultivada "in vitro": Datos concernientes a su histogénesis, Mem. r. Soc. españ. de hist. nat. **14**:123, 1930; Experimenteller Nachweis der morphologischen und funktionellen Eigenschaften und des mesodermischen Charakters der Mikroglia, Ztschr. f. d. ges. Neurol. u. Psychiat. **104**:371, 1930.

91. Costero, I.: Sobre los nódulos de Aschoff, in Libro Homenaje al Dr. I. Chávez, Inst. Nat. de cardiol. México, 1945.

logic reaction of importance in the nerve tissue. Other hemorrhages are due to diabrosis of the endothelium; they are predominantly of the annular type, and the extravasated red blood cells and necrobiotic zones are reabsorbed by compound granular cells. The entire process results in the formation of scars with aberrant nerve fibers, some hypertrophic fibrous astrocytes and slight proliferation of precollagenous fibers.

4. Possibly, the cerebral hemorrhages are responsible for the state of acute swelling of the brain which always accompanies, and frequently dominates, the cerebral edema.

5. It is difficult to find zones of entirely normal microglia in the wet brain of rheumatic patients. Commonly, the Hortega cells increase their cytoplasm and retract their expansions, and more of them than usual attach themselves to the capillaries; they also lose their characteristic spinous processes. These morphologic alterations of the microglia express profound and persistent metabolic changes in the brain of rheumatic fever.

6. Surrounding the areas of devastation, and in some apparently normal areas of the brain, the microglia acquires the modality of rod cells, while the same focus appears densely invaded by pseudopodal forms of microglia, a few hypertrophic fibrous astrocytes and nets of precollagen fibrils.

7. Among the frequent, but inconstant, complications in the brain of rheumatic patients there are meningoencephalic hemorrhages of greater extent than those described here, such as thrombosis and foci of softening.

8. Although none of the anatomic alterations aforementioned can be considered as specific for rheumatic fever, all of them taken together constitute an essential and constant component, indispensable to the understanding of the anatomic picture of rheumatic fever.

9. In the brain of some children who died of active rheumatic fever, I have found certain nodules of branching microglia cells, which originate in miliary foci of necrobiosis localized most commonly in the gray matter of the pons Varolii; the Hortega cells of these nodules soon undergo clasmatodendrosis and give place to small areas of demyelination, in which a few large neuroglia cells of the protoplasmic type are found. The nodules are not necessarily related either to the blood vessels or to any of the other lesions, and they disappear within a short time, without leaving a detectable connective tissue–vascular scar.

10. I consider it possible that the nodules of branching microglia cells represent a hyperergic reaction similar to that responsible for the Aschoff nodule in the connective tissue and that, therefore, they may be useful in the histopathologic diagnosis of the cerebral lesions during the evolutive period of rheumatic fever.

Calzada de la Piedad # 300.

INFLUENCE OF CHEMOTHERAPY ON THE PATHOLOGY OF PURULENT LEPTOMENINGITIS

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TORONTO, CANADA

THE EFFECT of penicillin and streptomycin on bacterial infections of the subarachnoid space has in general been beneficial, and the use of these agents by intrathecal administration has become widespread. A note of warning has been sounded by a number of authors,[1] who have described clinical examples of unfavorable results attributable to the direct toxic effect of penicillin or streptomycin on the cerebral tissues or their meningeal coverings. In experimental investigations, this direct effect of chemotherapeutic agents on the cerebral tissues has been studied carefully,[2] and the effect of penicillin on experimentally produced meningeal inflammations has also been evaluated.[3] There does not appear to have been any comment on the effect of penicillin and the other chemotherapeutic agents in altering or modifying the whole pathologic sequence of the development and resolution of human meningitides. With this end in view, a study was made of 16 cases of purulent meningitis treated by such agents, from the files of the department of

From the Division of Neuropathology, Department of Pathology, University of Toronto.

Read before the combined Sections of Pathology and of Neurology and Psychiatry of the Academy of Medicine, Toronto, March 19, 1948.

This paper is an abridgement of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Medicine (New Zealand).

1. Forrest, A. R.: Neurological Complications in Cerebrospinal Meningitis Treated with Penicillin, Brit. M. J. **2**:805-806 (Dec. 8) 1945. Stewart, H. H.: A Case of Paraplegia After Cerebrospinal Meningitis, ibid. **2**:319 (Sept. 8) 1945. Sweet, L. K.; Dumoff-Stanley, E.; Dowling, H. F., and Lepper, M. H.: The Treatment of Pneumococcic Meningitis with Penicillin, J. A. M. A. **127**:263-267 (Feb. 3) 1945. Siegal, S.: Tranverse Myelopathy Following Recovery from Pneumococcic Meningitis, ibid. **129**:547-550 (Oct. 20) 1945. Walker, A. E., and Johnson, H. C.: Penicillin in Neurology, Springfield, Ill., Charles C Thomas, Publisher, 1946.

2. Pilcher, C., and Meacham, W. F.: The Chemotherapy of Intracranial Infections. Treatment of Experimental Staphylococcic Meningitis with Intracranial Administration of Penicillin, J. A. M. A. **23**:330-332 (Oct. 9) 1943.

3. Pilcher, C., and Meacham, W. F.: The Chemotherapy of Intracranial Infections: Treatment of Pneumococcal Meningitis by Intrathecal Administration of Penicillin, J. Neurosurg. **1**:76-81 (Jan.) 1944.

neuropathology, University of Toronto, and the Hospital for Sick Children, Toronto. These cases were not studied from the point of view of the relation of treatment to the result in the individual patient; rather, the purpose was to obtain an over-all picture of the effect of the drug on the progress of the disease. To provide a standard of comparison, a similar survey was made of 46 cases from the department of neuropathology of persons who had died between 1932 and 1937, before specific treatment was employed.

OBSERVATIONS

From the comparison of these two series of cases certain observations were made. These will be discussed according to the tissue involved.

Effect on Pia-Arachnoid and Subarachnoid Exudate.—The removal of the subarachnoid exudate in purulent meningitis may be compared with the resolution of the exudate in lobar pneumonia. The liquefaction of exudate by ferments from disintegrating polymorphonuclear leukocytes appears to be of prime importance, while the accumulation of large mononuclear phagocytic cells in the vicinity of the pia mater also assists in the removal of debris (fig. 1 *A*). Further, the disintegration of the polymorphonuclear leukocytes may occur rapidly, beginning nearest the pia mater and affecting last the leukocytes under the arachnoid. In cases without treatment this process of massive necrosis appeared on the seventh day of the disease and was well advanced or completed by the tenth or twelfth day of the disease. In contrast, in the cases with treatment the necrosis of polymorphonuclear leukocytes in the exudate began more abruptly, on the fourth or fifth day, and was complete in most cases by the seventh day. This necrosis was not invariably accompanied with the liquefaction of the fibrin of the exudate, and it led to the accumulation of granular amorphous debris in the subarachnoid space. This debris was removed very slowly and was still to be seen as late as thirty-one and eighty-one days after the onset of the disease (fig. 1 *B*). The changes in the cerebrospinal fluid correlated closely with the aforenoted histologic findings in showing a prompt disappearance of polymorphonuclear leukocytes and bacteria and a slower disappearance of protein.

The possibility that organization may occur in the subarachnoid exudate was investigated. In the cases studied, any increase in the fibrous tissue was due to thickening and increase in density of the pia mater and arachnoid. In a number of instances there was localized fusion of these membranes, with obliteration of the subarachnoid space. In only 1 instance was there anything suggestive of granulation tissue in the subarachnoid space (fig. 2 *A*). Laidlaw's reticulum stain, as

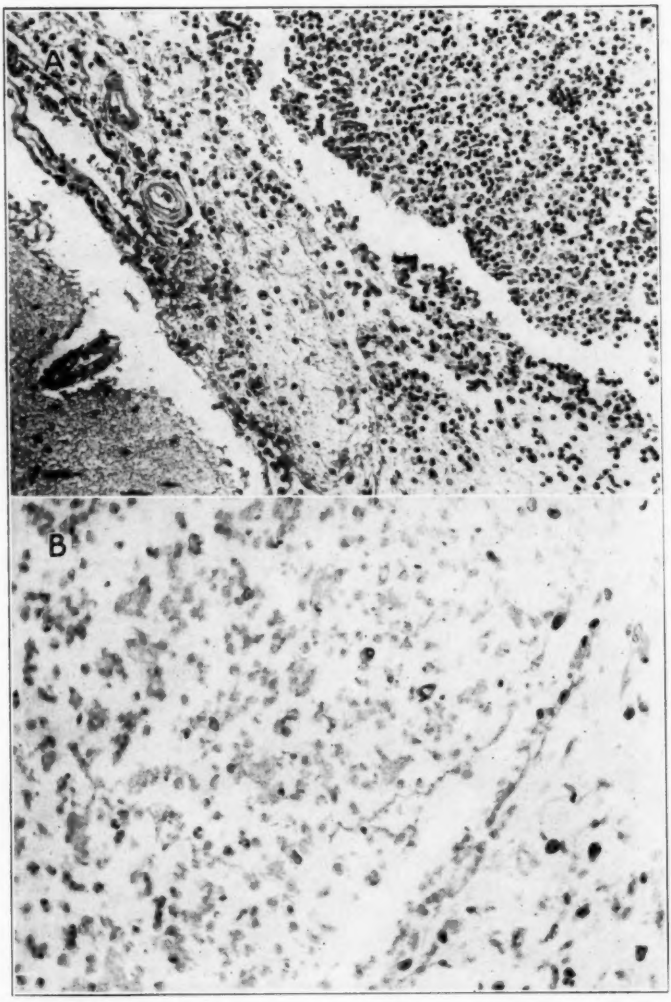

Fig. 1.—*A,* pneumococcic meningitis of three days' duration. The pia mater contains a cellular infiltrate, consisting of mononuclear histiocytes. There is a zone of fibrin, also containing mononuclear cells on its surface, while the exudate in the subarachnoid space consists almost entirely of polymorphonuclear leukocytes. Hematoxylin-eosin stain; × 155.

B, meningitis due to Pseudomonas aeruginosa treated with streptomycin, the patient dying thirty-one days after the onset of the disease. Note the almost complete cellular necrosis in the exudate with accumulation of cellular debris in the subarachnoid space. Hematoxylin-eosin stain; × 295.

The photomicrographs in this figure and in figures 2 and 3 are from the brains of treated patients.

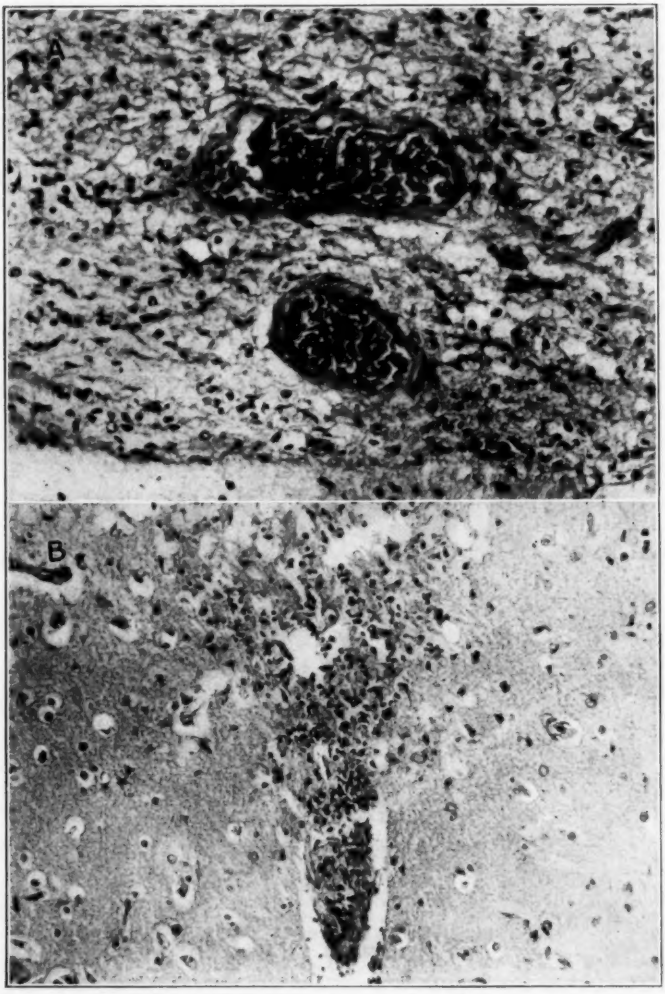

Fig. 2.—*A*, pneumococcic meningitis of eighty-one days' duration. The subarachnoid space is filled with organizing tissue, containing fibroblasts. Many collagenous fibers are forming. Two congested vessels are seen. The boundary between the pia mater and the marginal layer of the cerebral cortex (below) is well preserved in this area. Hematoxylin-eosin stain; × 265.

B, focal infective hemorrhagic lesion in a case of staphylococcic septicemia. A vessel in the deeper layers of the cortex has undergone thrombosis. As a result, there is a wedge-shaped area of acute necrosis of brain tissue with vacuolation and accumulation of polymorphonuclear leukocytes and some microglial cells. Hematoxylin-eosin stain; × 160.

used by Alpers and Forster[4] in studying subarachnoid hemorrhage, confirmed the observation that thickening of the arachnoid and pia was the main source of increased fibrous tissue, that the adventitial coats of subarachnoid vessels contributed little and that organization of the exudate was negligible.

Effect on the Cerebral Tissues and the Spinal Cord.—From comparison of the two series of cases, it appears that, although the changes in the substance of the brain and cord were similar in kind, they were less severe in the cases with treatment. The infection was localized strictly to the subarachnoid space in all cases, while the underlying brain showed a toxic reaction with some edema and neuronal degeneration. These changes were of an essentially reversible nature in the cases with treatment, whereas in the series without treatment the degeneration was observed to proceed in some cases to neuronophagia and disappearance of nerve cells.

An important type of localized lesions were observed in this series. These took the form of wedge-shaped areas of hemorrhage, local softenings and small abscesses (fig. 2*B*). In the great majority of cases these lesions were related either to vascular occlusion or to vascular spread of infected material. Lesions of this type were as frequently encountered in the control series as in the cases with treatment, but in the former group the lesions were more frequently observed in patients who died about the third week of the disease.

It was suggested by Cairns and Russell[5] that the frequency with which such local lesions are seen in the untreated patients who die about the third week, and the knowledge that penicillin treatment does not prevent the development of these hemorrhagic infarcts, should lead one to suspect that many recovered patients may have suffered minor or major insults of this character. In some of the cases studied such lesions were responsible for clinical neurologic signs.

Changes in the Cerebral and Meningeal Vessels.—The changes noted in the cerebral and meningeal vessels in the two series were comparable in nature and in degree. Three major vascular changes were noted: 1. Acute arteritis with subintimal inflammatory cell infiltrations. This change was observed in cases of seven days' duration or longer (fig. 3). 2. Fibrinoid necrosis of the tissues in the walls of the vessels, often associated with thrombosis of the affected vessels. This type of change is often seen in the white matter of the brain around an abscess, and it is also observed in a variety of other situations; from this occur-

4. Alpers, B. J., and Forster, F. M.: The Reparative Processes in Subarachnoid Haemorrhage, J. Neuropath. & Exper. Neurol. **4**:262-268 (July) 1945.

5. Cairns, H., and Russell, D. S.: Cerebral Arteritis and Phlebitis in Pneumococcal Meningitis, J. Path. & Bact. **58**:649-665 (Oct.) 1946.

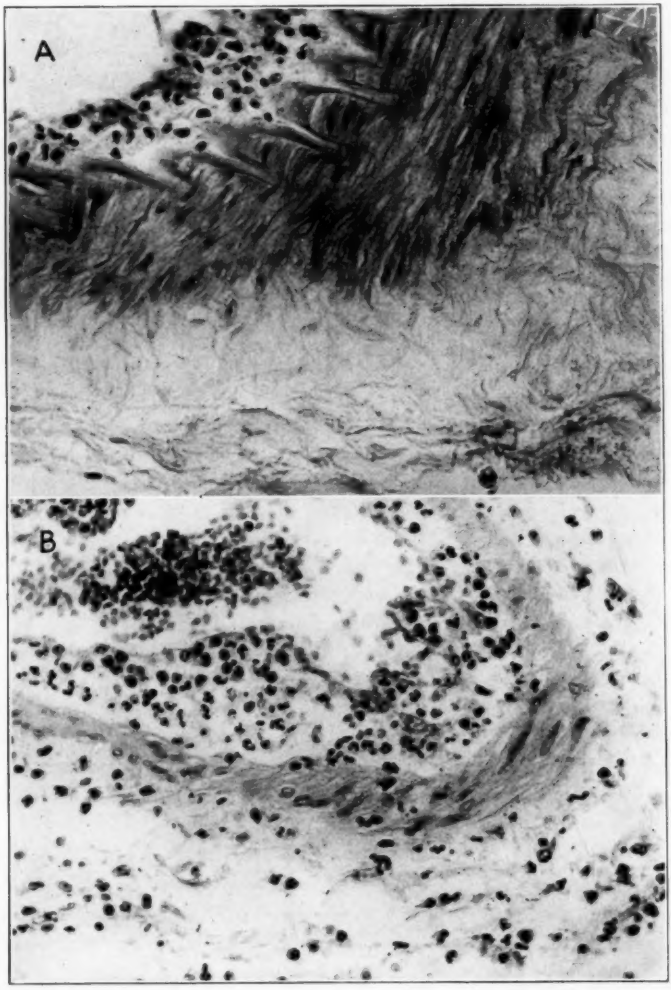

Fig. 3.—*A*, segment of a cortical artery in the subarachnoid space in a case of meningitis of seven days' duration. The subintimal collection of inflammatory cells is mostly mononuclear in type but a few polymorphonuclear leukocytes are seen. Note the absence of fiibroblastic proliferation in the adventitia. Hematoxylin-eosin stain; × 320.

B, superficial cortical artery in a case of pneumococcic meningitis of twenty-four days' duration. There are a subendothelial collection of inflammatory cells, including numerous polymorphonuclear leukocytes, and an accumulation of some inflammatory cells in the adventitia. Hematoxylin-eosin stain; × 295.

rence it may be concluded that this change is essentially a nonspecific one. 3. Fibrosis of the wall of some of the cortical vessels in the subarachnoid space, leading to a rigid, noncollapsible vessel.

Of these lesions, only the fibrinoid necrosis was associated with structural cerebral change, but whether it was the cause or the effect of the cerebral lesions noted in its vicinity is difficult to say.

The number of cases of long duration in this series is insufficient to permit comment on the opinion of Cairns and Russell [5] that the fibrinoid necrosis is a manifestation of an allergic response, such as was described by Ferraro.[6] While it cannot be denied that such an explanation may apply to some cases of one month's duration or more, it is evident in this series that there were other mechanisms by which such changes might be produced.

Changes in the Ependyma.—A significant difference was found in the degree of ependymal inflammation between the two series. Whereas in the cases without treatment perivascular collections of inflammatory cells, including polymorphonuclear leukocytes, were frequently seen, in the cases with treatment the perivascular collections were entirely lymphocytic. In both series the ependymal epithelium was preserved, but in a number of instances it was swollen and signs of desquamation were seen. The subependymal tissues were congested and edematous. These changes are undoubtedly due to the diffusion of bacterial toxins from the ventricular system. Two serious possibilities arise: (1) obstruction to the flow of cerebrospinal fluid by exudate in the aqueduct of Sylvius (fig. 4) or at the foramen of Munro, and (2) toxic damage to nuclei in the vicinity of the ventricles, especially the third ventricle, the aqueduct of Sylvius and fourth ventricle. The effect of chemotherapy in reducing the subependymal inflammation is therefore of great significance. It may also be regarded as a valid reason for the intraventricular administration of penicillin or streptomycin.

Changes in the Spinal Cord and the Cranial and Spinal Nerve Roots.—The changes observed in the spinal cord were essentially similar to those described in the substance of the brain. Of the few nerve roots available for examination, one showed an acute form of neuritis, with infiltration by polymorphonuclear leukocytes. No obvious differences were found between the series with and the series without treatment, and in only 1 instance was a meningeal reaction found which might be due to penicillin. No examples of arachnoiditis or radiculitis, complications frequently described in the literature, were encountered in these cases.

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6. Ferraro, A.: Vascular Changes in Experimental Anaphylaxis of the Brain, J. Neuropath. & Exper. Neurol. **4**:1-15 (Jan.) 1945.

Occurrence of Other Sequelae.—Other sequelae of meningitis for which no adequate pathologic explanation was found occurred among the treated patients. A patient known to be epileptic died in status epilepticus. This occurred while the infection was being brought under control with penicillin. It may be that the penicillin excited a cortex of low threshold to epileptic activity, or possibly it was unable to prevent the onset of epileptic seizures brought on by the infection. The known epileptogenic action of penicillin, as shown by Walker and associates,[7] was exhibited in another case in this series, in which the intrathecal administration of a concentrated solution brought on convulsions. While these 2 cases do not justify any conclusions, they at least suggest that one cannot expect a decrease in the incidence of the epileptic accompaniment of leptomeningitis with penicillin treatment.

Fig. 4.—Sagittal section of the brain stem and cerebellum in a case of meningitis due to Pseudomonas aeruginosa of thirty-one days' duration. Purulent exudate in the third ventricle and in the aqueduct of Sylvius had produced obstructive hydrocephalus.

Hydrocephalus of an obstructive type may result from obstruction at the level of the aqueduct or at the roof of the fourth ventricle. Penicillin treatment might, by bringing the ependymitis and meningitis more rapidly under control, prevent the development of this complication.

Generalized spasticity was a complication noted frequently by White and associates.[8] In only 1 case of this series was spasticity

7. Walker, A. E.; Johnson, H. C., and Kollros, J. J.: Penicillin Convulsions: Convulsive Effects of Penicillin Applied to the Cerebral Cortex of Monkeys and Man, Surg., Gynec. & Obst. **81**:692-701 (Dec.) 1945.

8. White, W. L.; Murphy, F. D.; Lockwood, J. S., and Flippin, H. F.: Penicillin in the Treatment of Pneumococcal, Meningococcal, Streptococcal and Staphylococcal Meningitis, Am. J. Med. Sc. **210**:1-17 (July) 1945.

emphasized as a clinical feature. A more extensive examination of the clinical histories of these patients might reveal other instances. In the 1 case of this series the spasticity may have been related to the severe hydrocephalus present.

SUMMARY

As a result of this study certain alterations in the pathologic process of the resolution of purulent meningitis with chemotherapy were noted. 1. Speeding up of bacterial destruction, with corresponding degeneration of the inflammatory cells of the exudate, may lead to clearing of cells from the cerebrospinal fluid, leaving a large amount of debris to be slowly removed from the subarachnoid space. Despite the presence of this fibrinous debris, organization of the exudate is unimportant as a complication. 2. The intensity of changes in the substance of the brain, especially in the subependymal tissues, is diminished. Vascular inflammation with, possibly, fibrinoid necrosis may, however, lead to focal infarction or hemorrhage. Adequate concentration of chemotherapeutic drugs in the ventricular system is essential to minimize the effects of the infection on the ependyma, and especially to prevent obstruction at any point in the ventricular system and to avoid toxic degeneration in subependymal nuclei. 3. Epileptic manifestations were present in 2 of 16 cases studied, an occurrence suggesting that there may not be any diminution in the epileptic accompaniment of purulent meningitis when chemotherapy is employed.

Dr. Eric A. Linell, Professor of Neuropathology, University of Toronto, gave helpful advice in the preparation of this paper.

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OBSERVATIONS ON CRIMINAL PATIENTS DURING NARCOANALYSIS

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NUMEROUS difficulties are encountered in diagnosing and treating a psychiatric patient who has been hospitalized through legal action because of criminal behavior. The precepts of therapy, which include (1) participation of the patient, (2) assistance to the patient in formulating for himself new, healthy attitudes in place of his unhealthy ones and (3) release of constructive elements of the personality rather than institution of changes by use of authority or pressure, are extremely difficult to attain. Zilboorg, in investigating the possibilities of psychotherapy with criminals in Sing Sing Prison, commented on the difficulty official prison physicians had in exerting true therapeutic influence on the prisoner.[1] The patient committed as criminally insane is faced with numerous barriers and restrictions placed there to minimize the possibilities of his escaping or doing harm to himself or to others. Despite progress in the direction of regarding criminal behavior as symptomatic of an underlying psychopathologic process, the usual attitude toward such a patient by those outside the hospital organization is that he is primarily a criminal and only secondarily a patient. This results in the genesis of a suspicious attitude on the part of the patient, if it is not already present, toward any one who is in a position of authority. It includes the doctor who is there for the purpose of administering psychotherapy, regardless of how well meaning he seems to the patient. From the beginning the patient is aware of the fact that the doctor in charge of his ward is responsible for discipline, general care and comfort and recommendations for disposition, in addition to his treatment.

Therefore, it takes considerable patience and reassurance to prepare a patient for the possible use of psychotherapy. Even after he is able to use therapy, and can be helped by it, the prospects of his utilizing the changes in himself may be limited. For instance, what is the use in helping a patient attain a heterosexual adjustment when it is obvious that he will be confined for a long time? Thus, not only must the preparation of the patient for therapy be considered but the goals of therapy have also to be evaluated carefully.

1. Zilboorg, G.: Investigative Therapy in Certain Types of Criminals, New York State J. Med. **43**:928, 1943.

Unlike the usual patient who seeks psychiatric help to live more comfortably, it is ordered by the court that the criminal patient have psychiatric care. It is true that the criminal patient is not considered legally responsible; but the fact remains that he is being commanded to accept something which he possibly does not desire. Although courts consider the wishes of patients who feel they need psychiatric help, the usual criminal is not seeking the kind of help the psychiatrist has to offer. This is analogous to the practice of certain well meaning physicians, social workers, school teachers and others in referring patients for psychotherapy who are obviously in great need of it but who do not especially want any help from a psychiatrist. Preparation of the patient so that he can use psychotherapy is in many instances a great undertaking in itself, just as is preparation of a patient for certain types of surgical procedure.

A great many of the criminal patients who were encountered were basically unaccepting of any extensive psychiatric help offered them. Ordinarily, the patient would oblige and be a "good patient," especially if he thought it would help him return to society. This is similar to the soldier who was cooperative with his medical officer if it meant being returned to the continental United States or medically surveyed from the service. Possibly, return to society is the first step that must be taken before help can be offered to such patients, as their confinement is an immediate and real problem. It is paramount in their minds and is a source of anxiety which acts as a barrier to any approach to the more long-standing conflictual material and emotional attitudes.

On the other hand, there are a number of patients who, although hospitalized as criminals, are receptive to therapy. This group should be treated selectively and more time spent on them than on the rest. In an effort to find a means of better diagnosis of the disturbances of these patients, narcoanalysis was used as an adjunctive aid [2]; being found useful, it was applied more extensively for purposes of observing to what use it could be put in areas other than mere diagnosis.

PRESENT INVESTIGATION

Observations on the use of narcoanalysis in a series of 50 patients at the Mendocino State Hospital, California, are presented. The patients were in the ward to which all male criminal patients in the state of California are sent for diagnosis and treatment, having been determined legally insane prior to admission. The group consisted of patients transferred from state prisons and those who were committed by the courts when acquitted by reason of insanity or whose trials were suspended because they were found to be presently insane. Patients were

2. Adatto, C. P.: Narcoanalysis as a Diagnostic Aid in Criminal Cases, J. Clin. Psychopath. **8**:4, 1947.

selected on the basis of presenting diagnostic problems or good therapeutic possibilities, as previously described.

After a preparatory phase of several interviews, the patient was told he would be narcoanalyzed for the purpose of being helped with his emotional difficulties and his consent was obtained. It was explained to the patient that he would feel intoxicated at first, that he would then have little memory of what went on and that he would awaken in a somewhat groggy state.

The technic of performing the narcoanalysis was as follows: When the patient was settled in a quiet room, a 10 per cent solution of thiopental sodium U. S. P. (sodium pentothal®) was gradually injected intravenously until a state of euphoria was reached. He was allowed to experience this for a while, and the conversation usually centered around how well he felt. After this he was asked some questions of a superficial nature, such as inquiries about his home town and school, and at the same time more thiopental was injected, until a deep phase was reached. This phase was characterized by slurred speech, nystagmus, yawning, long pauses in the stream of conversation and a tendency to fall asleep if conversation was not maintained. Whenever the patient was able he was allowed to ramble

Distribution of Diagnoses

	No. of Patients
Dementia precox	24
Psychopathic personality without psychosis	11
Undiagnosed psychosis	3
Without mental disorder	2
Psychosis with psychopathic personality	1
Post-traumatic psychosis	1
Alcoholic psychosis	1
Psychosis with convulsive disorder	1
Psychoneurosis, anxiety	1
Psychoneurosis, hysteria	1
Paranoid condition	1
Psychopathic personality with pathologic sexuality	1
Psychopathic personality with asocial trends	1
Psychosis with mental deficiency	1

on in a free manner, with the result that significant material was frequently produced. Then direct questions were asked the patient regarding his feeling about conflictual material, his legal difficulties, delusions, family situation, and the like, according to the nature of the case. To maintain the patient at a deep level of narcosis, the injection was continued, and finally he was allowed to become more conscious. Frequently this would precipitate another episode of free talking. When it was felt advisable that the patient integrate consciously what he was talking about, as in amnesia, he was allowed to become fully conscious before the interview was terminated. The average interview lasted about forty-five minutes. A stenogram of the interview was made in most cases in order that the material might better be evaluated and a record kept.

Of this group of patients, 20 were hospitalized and ordered to be returned to court to stand trial when they were considered no longer insane. Eighteen were acquitted of their crimes by reason of insanity and were legally able to be released at the end of one year of hospitalization if a court determined them to be sane at that time. Ten were transferred from state prisons because they were considered psychotic and were to be returned to prison when they recovered from their psychosis. One patient was legally classified as psychopathically delinquent and 1 as sexually psychopathic. The general tendency in all groups was for the patient to prove himself sane in order that he might be released from the hospital.

This tendency complicated an evaluation of the patient's diagnosis and therapeutic progress because of his wish to deny symptoms and present as favorable a clinical picture as possible.

Twelve of the group were veterans of World War II. Of these, 8 received medical discharges from the service because of neuropsychiatric disability, and the other 4 received either dishonorable or undesirable discharges. Six were given the diagnosis of psychopathic personality without psychosis; 5, of psychosis, and 1, of hysteria. It was observed that there was a tendency on the part of the courts to be lenient toward the veterans and to pronounce them insane in cases of doubt in order that they might receive psychiatric attention.

TRANSFERENCE

It is considered that the most important use of narcoanalysis in criminal cases is to break down resistance and aid in effecting a predominantly positive transference relationship. This is true only in that group of patients who are adequately prepared and willing to be narcoanalyzed. Unconditional acceptance of the patient's dilemma and needs is imperative before the patient will trust the psychiatrist and be willing to enter a relationship on a deep emotional level. Many patients are concealing something which they believe may incriminate them in future court action, and they feel it would be to their disadvantage to "open up." All too frequently they have experienced or heard of placing trust in an official and having the trust broken. Therefore, they enter a new relationship with extreme caution.

All the patients who were narcoanalyzed were motivated by a desire to help themselves in one way or another. Those who wanted help only in the area of release from the hospital and were evidently not concerned with their personality disturbances could be given little help. This group included persons with profound psychoses or deeply ingrained character disorders. Even though no transference relationship could be established with this group, a superficial friendly rapport could be attained which marked an advance, in that it was at least easier to get cooperation in their ward conduct.

Horsley [3] stated that sometimes a "negative transference" is apparent from the commencement of treatment, and in such cases there may be little or no progress in spite of every known therapeutic effort. "It is then that I have found it helpful to attempt to overcome the patient's unconscious resistance by means of narcoanalysis.[3] Freud [4] recognized the possibilities of using chemical agents to cope with certain psychologic forces. This method was found helpful with criminal patients

3. Horsley, J. S.: Narco-Analysis, London, Oxford University Press, 1943, p. 89.

4. Freud, S.: New Introductory Lectures, New York, W. W. Norton & Company, Inc., 1933, p. 211.

who exhibited anxiety, depression or concern over their plight beyond their feelings regarding their confinement in the hospital. It seemed that patients with little or no previous criminal or antisocial behavior were also more amenable to developing a positive transference via narcoanalysis. Frequently the transference was only a temporary event, which no longer existed once the patient was fully awake. How much therapy this resulted in is debatable. Probably it was dependent on the degree of state of narcosis and how much participation on a conscious level was involved. Usually in the ephemeral transference the patient was in a deep narcosis and the situation was analogous to a hypnotic state.

Kubie and Margolin [5] pointed out that under the influence of the drug an overt transference relationship may occur and that this relationship profoundly influences the data produced by the patient and his therapeutic integration of that data. This was exemplified in many of the cases under discussion by the use of the question "Tell me about your mother" while the patient was in a deep state of narcosis. Patients would frequently cry when talking about their mothers, and those who otherwise showed little affectivity would sometimes have an emotional catharsis while under thiopental narcosis. The following answers are examples: "Mother? She could have every last cent I got." (Crying) "I had the best mother in the world. I would lay down and die for her; but she is gone, she is gone." "My mother? She's swell." (Tears come to eyes) "She was a very, very good woman." (Cries) "My mother was a school teacher. I went to school." (Cries) "I wanted to be a decent sort of chap. I'm no stick-up man or nothing like that."

The guilt expressed by these patients and their frustration in attempts to obtain their mother's love became open. Occasionally feelings about the father would follow, as shown in the following verbatim recording:

Question: Tell me about your mother.

Answer: She is all right. She has lived a hard life. She has had a tough time. (Tears in eyes)

Question: Go on, tell me more about your mother. I am interested in her.

Answer: My father was a drunkard and I had to make the best of it. I went out and did do things, and work, and get stuff so we could eat, and get something to eat. (Cries and pauses)

Question: Go on.

Answer: That is why he died. He thought my mother was fooling around with a boarder we had in our house, and all the time he was mistaken, and he committed suicide. (Pauses) After that I went to work, and they wouldn't let me work, and so they sent me to the reform school. I wanted to work after that and they wouldn't let me. They kept fooling around and tried to make me go to school, and I finally gave up altogether. So I came back from the reform

5. Kubie, L. S., and Margolin, S.: The Therapeutic Role of Drugs in the Process of Repression, Dissociation and Synthesis, Psychosom. Med. **8**:3, 1945.

school and started working again, and my mother got married, and my step-father was always hard around the house, and calling everyone S. O. B., and I got tired and wouldn't take it any more, and told him to get the hell out, or something. And he called me "S. O. B." and I fought with him, and he wouldn't fight and I ran out of the house, and I left, and come out to California.

Question: Tell me more about your mother.

Answer: She is all right, but she blows up once in a while, because she has had such a hard life, and she didn't know what to do with herself half the time and the kids won't do anything for her. They won't help her with the housework, but it is on account of my step-father. He is all right in a way, but he is always hollering around the house, calling people "S. O. B." and I finally had to leave or something. I either had to leave, or I couldn't trust myself with him.

The patient for whom this interview was recorded murdered his wife because he was suspicious of her. He presented many paranoid ideas and considered me part of a group conspiring to keep him away from a fair retrial. Shortly after this interview, he exhibited his trust in me by bringing me voluntarily an implement he had concealed for the purpose of escaping. After that, we were able to discuss some of his feelings about people more openly, even though many of his ideas had a paranoid core. Although he was groping for help regarding his plight, he was never able to discuss emotionally charged feelings until his thiopental interview.

AMNESIA AND MALINGERING

Criminals often resort to amnesia, malingering and other feigned symptoms as a means of evading punishment. Malingering is one of the wastebaskets of classification of psychologic reactions, and the term as used here is confined to the deliberate production of symptoms with full knowledge of their origin. This is rarely seen; however, deliberate fabrication of symptoms is commonly observed in patients who are mentally ill. The differentiation from malingering is made on the basis that unconscious processes are to some extent producing this behavior in the patient. Most commonly in criminal cases this is seen as a symptom of a character disorder. Although one cannot call such a patient psychotic, one nevertheless must attempt to understand why it is necessary for such a person to feign symptoms. This phenomenon is also frequently seen in persons with incipient schizophrenia. One patient who was recovering from an acute schizophrenic break pretended to hear imaginary voices when confronted with a charge of theft. He had previously experienced true hallucinations and knew this was a part of insanity, which he was deliberately attempting to prove in order to avoid a penitentiary sentence. Under thiopental narcosis, he told how he feigned hallucinations so that he could protect himself because he felt that the hostile world was overwhelming him. He felt helpless and

unable to cope with his problem other than in this manner. It would be incorrect to call such a man a malingerer.

A panic state may result in an amnesia as a defense against being overwhelmed. This is a primitive defense mechanism and was commonly seen in the traumatic neuroses during the war. It is the person's way of protecting himself against overly painful stimuli which he cannot adequately handle. It is necessary for the psychiatrist to determine whether these reactions are part of a psychosis, another type of mental disorder or actual malingering. In the present series 16 patients presented an amnesia. Under thiopental narcosis, 7 were unable to recall any part of the amnesia, 7 had partial recollection and 2 had complete recollection. The manner in which they reacted to their amnesia under the influence of thiopental was significant. Patients with amnesias which were not feigned groped for an answer and were upset by not being able to recall. In discussing the events surrounding the period of amnesia, they would frequently become restless, perspire profusely, cry and show considerable emotional reaction. It was noted that in those who had partial recollection there was some symptomatic relief from anxiety. If the patient after being fully awake again had full amnesia, he was presented with the material he had brought out under narcosis with the explanation that he should know about what he discussed in order to make use of it if he could. Occasionaly this had the effect of an interpretation of feelings coming to the surface, and, as a result, the patient would consciously utilize the material, integrate it and substitute action for symptoms. A beneficial therapeutic effect was thereby effected.

An example of this observation is the case of a 30 year old man, white, married, whose trial, for assault and attempted rape on his sister-in-law, was suspended because he was found to be insane by the court alienists. He had complete amnesia for the episode with an accompanying fear reaction. On admission to the hospital he seemed to be almost completely overwhelmed by the situation, trusted no one and was fearful of talking lest he say the wrong thing. This resulted in his inability to discuss material other than that in the areas of his feelings of anxiety and fear. After a while he was told he might possibly be helped by narcoanalysis and he consented, with obvious reservations. Under thiopental narcosis, he gave a fairly coherent story of the incidents surrounding the assault and, with emotional catharsis, explained how his sister-in-law attempted to seduce him. When he accepted her advances, he was repulsed, and in a rage he attacked her. However, he was unable to carry the trend of conversation into the conscious area and when fully awake had no recollection of what he had said. Therefore, he was presented with the material he had related under narcosis. This resulted

in an intensification of his anxiety, and he expressed considerable concern about facing his wife and family, in addition to facing a possible prison sentence. This was discussed with him, as well as the various possibilities of what might happen to him, in order to help him return to the reality of his situation. Several days later he came in voluntarily and talked about the whole event in detail, with the release of a considerable amount of hostility to his sister-in-law. He then stated how relieved he was because he knew he should return to court, face his family and, as he put it, "face the music." Anxiety was dispelled when he used conscious judgment to solve his problem. No attempt was made to go into the more underlying reasons for having sexual feelings toward his sister-in-law because it was felt this would actually be detrimental to therapy by uncovering conflictual material which he might not be able to handle. It is interesting to speculate that he might have been acting out incestuous feelings regarding his sister or mother. This possibility was not explored because it was thought that anxieties might be aroused which it would take a long time to work through. It seemed that his return to court, so that he could solve his immediate problem, was more important therapeutically than the benefits of further therapy at that time. This man was probably never psychotic but, nevertheless, was in need of psychiatric help to overcome his near-panic state. It was considered that narcoanalysis helped speed this man's recovery from his immediate problem.

DELUSIONS AND HALLUCINATIONS

Another group of patients was narcoanalyzed to ascertain whether or not hallucinations and delusions were still present. Psychotic patients with superficial insight would calculate that the only way in which they could be released from the hospital was to deny their symptoms. Hence, they would resort to saying they no longer heard voices or would talk about their previous delusions as something "foolish." Kalinowsky and Hoch [6] pointed out that under sodium amytal narcosis delusions and hallucinations can be elicited which were not previously disclosed. The value of this procedure except for diagnosis is questionable. It may be said, on the other hand, that suppression of delusions is a form of resistance to therapy and that breaking down of this barrier may help with the course of therapy. Seven patients who were considered to be clinically psychotic had a recurrence, in part or whole, of their delusions or hallucinations while under thiopental narcosis. Three retained their delusions and hallucinations on awaking, while the other 4 continued to

6. Kalinowsky, L. B., and Hoch, H.: Shock Treatments and Other Somatic Procedures in Psychiatry, New York, Grune & Stratton, Inc., 1946, p. 201.

deny them. In addition to the deliberate denial of their feelings, the possibilities of deterioration, on the one hand, and of suppression or repression as a result of recovery, on the other, should be considered.

A case to exemplify this is that of a white man aged 33 who was transferred from San Quentin Prison because he was considered psychotic, as evidenced by hallucinatory experiences involving his wife. He had a history of five previous arrests and was incarcerated in prison for burglary. On admission to the hospital, he denied having any hallucinations, despite the fact that it was pointed out to him that these were recorded in his prison medical report. It was difficult to evaluate his condition because, except for a general vagueness in his ideation, there were no evidences of a frank psychosis. Under thiopental narcosis he was at first reluctant to discuss his hallucinations, but after a while he related them in detail. He explained how he heard his wife speak to him day and night and how she did everything to annoy him. Also, he told of how some movie actresses were bothering him with messages, elaborating with: "That's the main reason why I'm so underweight now. I couldn't sleep day and night. I couldn't sit down and partake of a meal without them pestering and annoying me. He's doing this; he's doing that." Accompanying this was an intense reaction of fear and anxiety. When he became fully conscious, he could not recall the experiences which he discussed under thiopental narcosis and stated that he was aware he had some disturbing ideas but could not quite explain them. It was felt that this man was in the process of repressing a psychotic episode and that therapy should proceed, with the aim of helping him with his repressive process, as follows: No further discussion was centered about his hallucinations, and he was not presented with the material he discussed. His vagueness later disappeared, and in due time he was returned to prison as recovered from his psychosis.

FABRICATED STORIES

Popularly, barbiturates given intravenously are known as the "truth serum," with the implication that the subjects on whom they are used will always tell the truth. Ripley and Wolf [7] noted that some patients deliberately misrepresented facts while under the influence of sodium amytal. In this group 3 patients fabricated new stories while under thiopental narcosis. All were persons who told stories regarding overseas heroism during the war, although, as proved later by themselves, they were not involved in any such action. All had been fabricating stories prior to being narcoanalyzed and merely continued the same trend

7. Ripley, H. S., and Wolf, S.: Intravenous Use of Sodium Amytal in Psychosomatic Disorders, Psychosom. Med. **9**:4, 1947.

while under deep narcosis. When asked why they fabricated stories, they commonly replied that nobody believed them anyway and they might as well continue doing it. It was not possible to establish more than a superficial relationship with these patients, and the reasons for their distrust were probably deeply repressed.

A Mexican-American man with grandiose ideas while under thiopental narcosis told of being in the espionage service in the Army, assigned to find out what certain ships were doing in Pearl Harbor in 1940. He told of how he found out that the Japanese and Germans were taking soundings of the harbor and that he was appointed for the assignment "because of my character and my eyes matching the Orient." He told of receiving advanced degrees from Canton University, in China, and also from the University of Santo Tomas, in Manila. While expressing his feelings about the persecution of the Chinese by the Japanese, he became apprehensive and fearful. Also, he told of how unworthy he considered himself as a husband and how badly his father treated his mother. After discussing both his wife and mother, he was asked whether his wife reminded him of his mother. He replied "Yes, she was true to me, just like my mother. [Long pause] My mother had some money for me, and my step-father stole it from her." His crime was issuing checks without sufficient funds. Under thiopental narcosis, he effected a transference, but afterward he resumed fabricating stories, became openly hostile toward every one in the hospital and was not amenable to therapy.

COMMENT

The consistency with which these men, charged with criminality and found to be mentally ill, had abreactions under thiopental narcosis in the areas of discussion surrounding their mothers is worthy of note. Also, the hostility which some expressed toward their fathers, and with greater intensity toward father-substitutes, should be mentioned. The type of crime committed could frequently be tied in with the nature of the relationship they had with their parents and parent-substitutes. Clues to the nature of the conflictual material in some of these patients could frequently be found in the type of offense which they committed repeatedly in a compulsive manner. It is felt that this material is further evidence of the view that conflicts in early childhood are perhaps the very basis of the concept of crime. Narcoanalysis can serve as a further means of research regarding the psychologic origin of crime, because patients under narcosis elicit emotionally charged material which they do not or cannot discuss while fully awake.

SUMMARY

In an effort to break down barriers which exist in giving psychotherapy to criminal patients who are hospitalized for the purposes of diagnosis and treatment of mental illness, narcoanalysis was used. Comments on a group of 50 such patients who were narcoanalyzed are presented. It is felt that the most important use of intravenously administered barbiturates in the treatment of these patients is the way in which it breaks down resistance and helps in establishing a predominantly positive transference. The problems of amnesias, malingering, delusions, hallucinations and fabrication of stories under narcoanalysis are also discussed.

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NEOSTIGMINE METHYLSULFATE THERAPY IN HEMIPLEGIA

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AFTER Loewi's [1] (1932-1933) monumental discovery of neurohumoral mechanisms in 1921, many efforts were made to study the effect of cholinergic drugs on neuromuscular disorders. Sciclounoff [2] (1934) found that acetylcholine chlorohydrate hastened improvement in hemiplegia, while Ward and Kennard [3] (1942) reported that strychnine, thiamine hydrochloride and carbaminoylcholine facilitated recovery of hemiplegia produced in monkeys by cortical ablation. Carbaminoylcholine chloride gave the best results. Kremer [4] (1942) studied the effect of intraspinal injection of neostigmine methylsulfate on hemiplegia and found that it caused a diminution of tone and of both normal and abnormal reflexes. He also observed a decrease in the power of voluntary muscles on the hemiplegic side.

Kabat and Knapp [5] (1943) described beneficial effects with neostigmine on muscular spasm in poliomyelitis. Later, Kabat [6] (1944)

Hoffmann-LaRoche, Inc., made available liberal amounts of neostigmine (prostigmin®) for these studies.

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Dr. A. McGehee Harvey, Physician in Chief, the Johns Hopkins Hospital, gave helpful criticism in the preparation of this publication.

1. Loewi, O.: The Humoral Transmission of Nervous Impulses, Harvey Lectures, Baltimore, Williams & Wilkins Company, 1933, series 28, pp. 218-233.

2. Sciclounoff, F.: L'acétylocholine dans le traitement de l'ictus hémiplégique, Presse méd. **42**:1140-1142, 1934, cited by Ward and Kennard.[3]

3. Ward, A. A., and Kennard, M. A.: Effect of Cholinergic Drugs on Recovery of Function Following Lesions of the Central Nervous System in Monkeys, Yale J. Biol. Med. **15**:189-228, 1943.

4. Kremer, M.: Action of Intrathecally Injected Prostigmine, Acetylcholine, and Eserine on the Central Nervous System in Man, Quart. J. Exper. Physiol. **31**:337-357, 1942.

5. Kabat, H., and Knapp, M. E.: The Use of Prostigmine in the Treatment of Poliomyelitis, J. A. M. A. **122**:989 (Aug. 7) 1943.

6. Kabat, H.: Studies on Neuromuscular Dysfunction: I. Neostigmine Therapy of Neuromuscular Dysfunction Resulting from Trauma; II. Neostigmine Therapy of Hemiplegia, Facial Paralysis, and Cerebral Palsy; III. Neostigmine Therapy of Chronic Rheumatoid Arthritis and Subcromial Bursitis, Pub. Health Rep. **59**:1635-1650, 1944.

applied this drug more widely and included in his study "neuromuscular dysfunction resulting from trauma," hemiplegia, facial paralysis, cerebral palsy, chronic rheumatoid arthritis and subacromial bursitis. He reported definite improvement in this great variety of diseases. In the light of the negative results obtained in the present studies it is important to indicate that Balboni, Hollander and Kydd [7] (1946) obtained no beneficial effects in 23 cases of rheumatoid arthritis. Schlesinger referred to the presentation of the findings of Balboni and associates at the meeting of the American Rheumatism Association in May 1946, and pointed out that the negative results of these authors had strong support.

It is pertinent to refer in greater detail to some of Kabat's [6] (1944) observations on hemiplegic patients. He treated 7 patients with the duration of illness varying from three months to seventeen years. Improvement, Kabat stated, could be observed twenty-four hours after treatment with neostigmine methylsulfate was started. The patient with a condition of seventeen years' duration responded with marked improvement in muscular strength and joint mobility, and long-standing deformities were corrected. Kabat's observations stand in contrast to Kremer's [4] in that the latter observed increased tone and reflex activity with muscular twitchings as the result of intramuscular or intravenous administration of neostigmine. While Kremer produced a decrease of tone and reflex activity with intrathecal injection of neostigmine, such as Kabat obtained with subcutaneous injection of the drug, he reported loss of muscular power, rather than the increase in strength described by Kabat.

In a second report, Kabat and Jones [8] (1946) confirmed Kabat's observations, while Schaubel [9] (1944) treated children with spastic cerebral palsy with neostigmine and obtained beneficial results. Kabat [10] (1947) extended his observations to multiple sclerosis and reported that neostigmine therapy and intensive muscular reeducation were "highly effective." In these studies the improvement reported could hardly be ascribed specifically to the neostigmine because of the factor of reeducation in the treatment. That Kabat's universally good results

7. Balboni, V. G.; Hollander, J. L., and Kydd, D. M.: The Effect of Prostigmine (Neostigmine) on the Muscle Spasm of Rheumatoid Arthritis, Am. J. M. Sc. **212**:153-158, 1946.

8. Kabat, H., and Jones, C. W.: Studies on Neuromuscular Dysfunction, J. Nerv. & Ment. Dis. **103**:107-128, 1946.

9. Schaubel, H. J.: Prostigmine As an Adjunct in the Treatment of Spastic Cerebral Palsy, Physiotherap. Rev. **24**:236-237, 1944.

10. Kabat, H.: Studies of Neuromuscular Dysfunction: X. Treatment of Chronic Multiple Sclerosis with Neostigmine and Intensive Muscle Re-Education, Permanente Found. M. Bull. **5**:1-14, 1947.

with neostigmine in treatment of neuromuscular disorders are probably due to an inadequately critical approach to the problem is indicated by Schwab and Chapman [11] (1947), who stated that at a number of orthopedic centers in New York, Chicago, Boston and St. Louis they have treated "spastic states" with neostigmine but have given it up. Schwab and Chapman also referred to observations carried out by one of them in 12 cases of spastic paralysis, with no objective improvement evident. These observations were carefully controlled and checked by means of ergographic, electromyographic and neurologic studies.

MATERIAL AND METHOD

Ten cases of hemiplegia of variable duration—eight months, one year two months, one year nine months, two years, two years, three years, four years, five years, nineteen years and unknown, were included in this study The cause in all cases was cerebral vascular thrombosis, due either to arteriosclerosis or to syphilis. Each patient was examined for deformity, active mobility and passive mobility of the limbs, muscle strength and muscle tone. Deformity, active mobility and passive mobility were measured in degrees. Increase in tone and loss of strength were evaluated as follows: 0, normal; 0.5, slight; 1, mild; 2, moderate; 3, marked, and 4, complete loss of strength or extreme increase in tone. Complete loss of active or passive mobility was rated as 4, also.

After control observations were made, the patients were given injections of sterile water three times a day for periods varying from eight to twenty-one days. After this they were reexamined, and the neostigmine methylsulfate, 1 or 1.5 mg., and atropine sulfate, 0.65 to 0.43 mg. (1/100 or 1/150 grain), were administered intramuscularly three times a day for thirty-one to sixty-five days. The patients were reexamined at least once during the interval of treatment and at its termination.

Although no other treatment was given during the period of observation, a number of the patients, stimulated by the interest shown in them, began to indulge in exercise and passive manipulation of the involved limbs.

OBSERVATIONS

Since the results in the 10 cases were similar, the data on 1 case only are presented in detail in the table, and only the data pertaining to abnormalities are included. The last two columns of the table show the effects of the placebo and of neostigmine, respectively, on the various abnormalities.

It is evident from the data presented in the table that whatever improvement occurred during administration of neostigmine was no greater than that observed during the control (placebo) period. As a whole, the effects of neostigmine therapy were as often increases in the degree of abnormality as improvements. In the case for which

11. Schwab, R. S., and Chapman, W. P.: Clinical Uses of Neostigmine, M. Clin. North America **31**:1238-1260, 1947.

Abnormality	Descriptive Type †	Aug. 9	Aug. 21	Sept. 6	Oct. 9	Improvement: Placebo	Improvement: Neostigmine
Deformity ‡							
Mouth	Dep	0.5	0.5	0.5	0.5	0	0
Neck	R	10°	0	0	0	+10°	0
Shoulder	El	0	0.5″	..	0.5″	−0.5″	0
Elbow	E	180°	180°	180°	175°	0	+50
	P	130°	130°	135°	135°	0	−50
Wrist	F	160°	160°	160°	155°	0	−50
	Ab	10°	0	5°	0	+10°	0
Fingers	F	MP PI DI	....	....	....	...	....
	1	180° 90°	....	....	....	...	....
	2	135° 90° 135°	....	....	....	...	....
	3	135° 90° 135°	Same	Same	Same	0	0
	4	135° 90° 135°	....	....	....	...	....
	5	135° 90° 135°	....	....	....	...	....
Ankle	E	.....	150°(L=130°)	150°	155°	...	−5°
	IR	R sl. > L	R 15° > L	Same	Same	0	0
Toes	E	R 20° > L	R 45° > L	R 25° > L	R 45° > L	−25°	0
Active Mobility							
Mouth	Lag	0.5	0.5	0.5	0.5	0	0
Neck	Ab	?	20°	30°	25°	?	+5°
	R	50°	55°	60°	60°	+5°	+5°
Shoulder	Total	4	4	4	4	0	0
Elbow	Total	4	4	4	4	0	0
Wrist	Total	4	4	4	4	0	0
Fingers	Total	4	4	4	4	0	0
Hip	F	90°	80°	90°	85°	+10°	−5°
	Ab	10°	0	15°	20°	+10°	?
	IR	25°	30°	30°	10°	+5°	−20°
	ER	15°	15°	15°	30°	0	+15°
Knee	F	80°	90°	80°	60°	−10°	+30°
Ankle	Total	4	4	4	4	0	0
Toes	Total	4	4	4	4	0	0
Passive Mobility							
Shoulder	Ab	80° pain	90° p	80° p	90° p	+5°	0
	F	100° p	95° p	90° p	90° p	−5°	−5°
Elbow	F	120° p	120° p	120° p	120° p	0	0
	P	180°	180°	180°	180°	0	0
Wrist	E	135° p	130° p	130° p	135° p	−5°	+5°
Ankle	F and E	10°	10°	5°	5°	0	−5°
Strength							
Neck	Ab	?	0.5	0.5	2	?	−1.5
	R	3	2	1	2	+1	0
Shoulder	Total	4	4	4	4	0	0
Elbow	Total	4	4	4	4	0	0
Wrist	Total	4	4	4	4	0	0
Finger	Total	4	4	4	4	0	0
Hip	F	0.5	2	2	2	−1.5	0
	E	2.5	2	3	2	+0.5	0
	Ab	3	2	2	2	+1	0
	Ad	0	2	0.5	0.5	−2	+1.5
	IR	3	2.5	2	3.5	+0.5	−1
	ER	3	2.5	2	2.5	+0.5	0
Knee	F	1	1	1	1	0	0
	E	1	0.5	1	1	+0.5	−0.5
Ankle	Total	4	4	4	4	0	0
Toes	Total	4	4	4	4	0	0
Tone							
Neck	Ab	0	0	0.5	0	0	0
	R	0	0	0.5	0.5	0	−0.5
Shoulder	Ab	2	2	1.5	2	0	0
	F	3	3.5	3.5	3	−0.5	+0.5
	E	2	1	1.5	2	+1	−1
Elbow	F	2	1.5	2.5 pain	2	+0.5	−0.5
	E	1	0.5	1	0.5	+0.5	0
	P	0	0.5	0.5	0.5	−0.5	0
	S	2.5	1.5	2	2.5	+1	−1
Wrist	F	0	0	0.5	0.5	0	−0.5
	E	1	1	1	2.5	0	−1.5
Fingers	E	0.5	1.5	0.5	0.5	−1	+1
Hip	Ab	1.5	0	0.5	1	+1.5	−1
Knee	F	1	1	1	1	0	0
	E	1	0.5	1	1	+0.5	−0.5
Ankle		Marked rigidity of joints					
Toes	E	0	1	..	1.5	−1	−0.5

* The status of the patient's abnormalities is represented as determined prior to placebo administration, August 9; at the termination of placebo administration and just prior to administration of neostigmine and atropine, August 21; during the course of treatment with the latter drugs, September 6, and at the time of discontinuation of the drugs, October 9. The amount of improvement noted during the course of placebo administration and that of treatment with neostigmine is represented in the last two columns by means of positive values. Any aggravation of the abnormalities is represented by a negative value. No change is indicated by a zero.

† The abbreviations in this column are: Ab, abduction; Ad, adduction; Dep, depression; E, extension; El, elevation; ER, external rotation; F, flexion; IR, internal rotation; P, pronation; R, rotation; S, supination; Total, all movements. Under "fingers," numbers 1 to 5 refer to the digits.

‡ Under the heading "deformity," the angle of deformity is recorded. Under "active mobility," the angle produced by maximum movement is indicated. Complete paralysis is indicated by the numeral 4. Under "passive mobility," the angle resulting from maximum passive movement is given, and the letter p refers to pain resulting from this movement. The degree of "loss of strength" and increase in "tone" is recorded as follows: normal, 0; slight, 0.5; mild, 1; moderate, 2; marked, 3; complete or extreme, 4.

data are presented in the table there were 9 positive values or improvements and 19 negative values, indicating increased abnormality. In another case there were 22 positive and 17 negative values. In addition to the negative results referred to, there was complete failure of the treatment to afford relief from any pain caused by manipulation of the involved limbs. It is obvious that the changes observed during administration of neostigmine are not significant and fall within the range of the normal variations that occurred in the patients studied.

COMMENT

In evaluating the effect of a therapeutic agent on a condition that varies from time to time, it is vital that one be informed on the range of this variation before the effect of any treatment procedure can be determined. The degree of disability in hemiparesis is not rigidly constant. The range of passive movement, which is probably less likely to vary than the other modalities tested, is not completely invariable, unless it is limited by an absolutely fixed joint. If the threshold to pain on motion of a joint varies, then the range of movement allowed will vary to the same degree. In addition, the examiner's response to the patient's pain is variable. How much pain evinced by the patient is a signal for the examiner to discontinue the mobilization of the paretic limb? A variation of 10 to 15 degrees is easily introduced by these factors. Balboni and associates pointed out that the error in goniometric measurements is of the order of 10 to 15 degrees.

The errors intrinsic in assessing active mobility are even greater, for this estimate requires the full cooperation of the patient at all times. The phenomenon of associated movement must also be carefully judged. When a patient attempts to move a paretic limb, the latter may move in association with activity inadvertently induced in other parts of the body, such as occurs during straining, rather than because of the intention of the patient. In a number of instances, seemingly voluntary, active mobility was ultimately found to be associated, rather than primary, in nature.

The judgment of changes in muscle tone in disease of the pyramidal tracts is not a simple procedure because of the lack of constancy in the increased tone throughout the range of passive movement. The muscle may be completely relaxed through a segment of the range of movement and then the tone suddenly become exaggerated, to offer greater resistance to the examiner. This introduces disconcerting variations.

The testing of muscle strength by judging the resistance sensed by the examiner, as in testing tone, is only a crude quantitative measure. Two persons might vary considerably in assessing the strength or tone

of a particular muscle group. Moreover, when tone is greatly increased, the resistance offered by the increased tone may be mistaken for muscle strength.

This reference to several of the sources of error which may interfere with a precise evaluation of the degree of disability present in hemiplegic persons should afford a basis for understanding, at least partially, the variability that occurs in the abnormalities studied.

CONCLUSION

Neostigmine methylsulfate administered intramuscularly had no significant beneficial effect in 10 cases of hemiplegia.

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PLASMA CALCIUM FRACTIONS AFTER ELECTRIC CONVULSION TREATMENT

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INVESTIGATIONS of the blood chemistry during electric convulsion treatment have shown varying results, owing to the fact that the analyses have been made at different times after the convulsion. The ion balance, with particular reference to calcium, has been a point of especial interest. Delay and Soulairac [1] in 4 cases reported an average increase of about 23 per cent in the blood calcium after an electric convulsion treatment. The blood was taken in these cases immediately before and ten minutes after the electrically induced convulsion. On the other hand, Katzenelbogen, Baur and Coyne [2] found an increase in the blood calcium content in 27 of 41 patients, while 13 patients showed a decrease and 1 patient had no change after electric shock. However, these investigators took the blood within eighty-six minutes after the convulsion, indicating no standard time for withdrawal of blood, so that it is difficult to interpret their results.

Blood proteins were found to increase 7 to 20 per cent within one to two minutes after an electrically induced grand mal convulsion,[3] and, since it is known that the nonultrafiltrable calcium fraction, which comprises 40 to 60 per cent of the total blood calcium, exists largely in combination with plasma proteins, we wondered whether the alleged increase in blood calcium immediately following an electric convulsive treatment could be attributed solely to the nonultrafiltrable calcium fraction. On the other hand, however, the possibility existed that the amount of calcium was increased equally in each fraction, i. e.,

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1. Delay, J., and Soulairac, A.: Variations du calcium et du phosphore minéral sanguins après l'électrochoc, Compt. rend. Soc. de biol. **137**:383-384, 1943.

2. Katzenelbogen, S.; Baur, A. K., and Coyne, A. R. M.: Electric Shock Therapy: Clinical, Biochemical and Morphologic Studies, Arch. Neurol. & Psychiat. **52**:323-326 (Oct.) 1944.

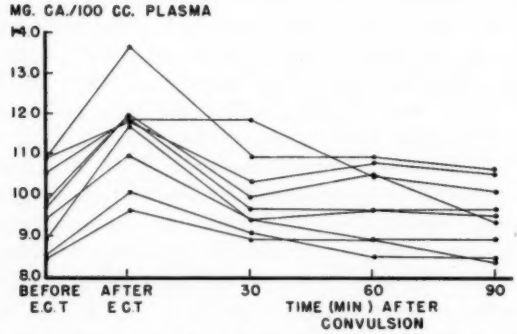
3. Horwitz, W. A.; Sperry, W. M., and Barrera, S. E.: Proc. Am. Psychiat. A., 1943, p. 28; cited by Horwitz and Sperry.[4]

ultrafiltrable and nonultrafiltrable, thus lending support to the hemoconcentration theory of Horwitz and Sperry,[4] who claimed that this phenomenon occurs after an electrically induced grand mal convulsion.

The purpose of this investigation, then, was to determine whether the blood calcium increases after an electric convulsive treatment and, if it does, at what time the calcium returns to the preshock level. In addition, a study of the ultrafiltrable and nonultrafiltrable plasma calcium fractions and, to a lesser extent, of the plasma proteins before and after shock therapy was undertaken.

EXPERIMENTAL METHOD

Calcium analyses were performed on the plasma of 22 unselected psychiatric patients immediately before and immediately after an electric convulsion treatment. In 9 additional patients the plasma calcium levels were determined immediately



Total plasma calcium levels immediately before, immediately after and for ninety minutes after electric-convulsive treatment.

before and after the shock and at certain intervals within a period of one and a half hours after the convulsion.

Ultrafiltrations of the plasma of 7 other patients before and after shock were carried out, and the ultrafiltrable and the total plasma calcium were determined. Data on the nonultrafiltrable calcium fraction were obtained as the difference between the value for total plasma calcium and that for the ultrafiltrable calcium fraction. The ultrafiltration was accomplished with a modification of the apparatus described by Greenberg and Gunther.[5]

In all cases the calcium of the plasma of heparinized blood was determined according to the titrimetric method of Salomon, Gabrio and Smith.[6] It was

4. Horwitz, W. A., and Sperry, W. M.: Biochemical Changes in the Blood Following Electric Shock Therapy, Federation Proc. **6**:263 (March) 1947.

5. Greenberg, D. M., and Gunther, L.: On the Determination of Diffusible and Non-Diffusible Serum Calcium, J. Biol. Chem. **85**:491-508 (Jan.) 1930.

6. Salomon, K.; Gabrio, B. W., and Smith, G. F.: A Precision Method for the Quantitative Determination of Calcium in Blood Plasma, Arch. Biochem. **11**: 433-443 (Nov.) 1946.

found in preliminary experiments that a minute amount of liquid heparin did not interfere with the quantitative procedure employed.

Plasma protein concentrations of 2 patients immediately before and after shock were calculated from nitrogen determinations made by the micro-Kjeldahl method, using a copper-selenium catalyst.

Electrophoretic patterns[7] of the plasma of 1 patient were obtained immediately before and after an electric convulsive treatment. Electrophoresis was carried out in the tall form of the standard 11 ml. Tiselius cell, employing veronal® (barbital U.S.P.) buffer with a p_H 8.5 and an ionic strength 0.1. The patterns were photographed by the scanning method of Longsworth,[8] and the areas of the peaks were obtained from photographic enlargements by the use of a planimeter. The hematocrit readings of 5 additional patients immediately before and after convulsions were determined with the use of Wintrobe tubes.

All the patients studied experienced grand mal convulsions during the electric convulsion treatments.

RESULTS AND COMMENT

An examination of the results of determinations of plasma calcium levels immediately before and immediately after electric convulsion

TABLE 1.—*Ratio of Differences Between Mean Plasma Calcium Levels Immediately Before and Immediately After Electric Convulsion Treatment as Shown in the "Student" t Test*

Group	N	Mean	σ	$M_A - M_B$	t	P
Before electric convulsion.....	22	10.00	0.757	1.52	4.76	<0.01
After electric convulsion.....	22	11.52	1.293			

treatment shows that in each of the 22 cases the calcium content had increased about 7 to 25 per cent, with an average increase of 15.2 per cent. The calcium values before shock ranged from 8.77 to 12.37 mg. per hundred cubic centimeters, the average value being 10.00 mg. After the treatment the calcium content ranged from 10.03 to 16.31 mg. per hundred cubic centimeters, with an average of 11.52 mg. The data were subjected to the Student t test (table 1), and a highly significant difference statistically between the mean plasma calcium values of the two groups was found ($P < 0.01$).

In the accompanying chart, the total plasma calcium values immediately before and after and for ninety minutes after the shock are plotted. In all 9 cases the calcium had returned to the preconvulsion level, or slightly below, within ninety minutes after the treatment. It may be noticed, however, that within thirty minutes after the

7. Dr. E. L. Alling, of the Departments of Radiology and Medicine, University of Rochester School of Medicine, Rochester, N. Y., made the electrophoretic analyses.

8. Longsworth, L. G.: A Modification of the Schlieren Method for Use in Electrophoretic Analysis, J. Am. Chem. Soc. **61**:529-530 (Feb.) 1939.

convulsion the preshock level had been reached in 4 of the patients. In view of these results and those presented in table 1, one may conclude that there is an initial increase in the total calcium of the plasma immediately after an electrically induced convulsion, followed by a gradual decrease, which varies with the patient, reaching the preconvulsion level or slightly lower within ninety minutes after the convulsion. Since Katzenelbogen and associates [2] took their samples of blood within eighty-six minutes after the convulsion and presumably took only one postconvulsion sample for each patient, it is understandable that they found an increased blood calcium in some patients, a decrease in others and no change in 1 subject, the value depending on the time of withdrawal of blood after the convulsion.

TABLE 2.—*Total, Ultrafiltrable and Nonultrafiltrable Plasma Calcium Levels Immediately Before and Immediately After Electric Convulsion Treatment*

		Total Plasma Calcium, Mg./100 Cc.		Ultrafiltrable Plasma Calcium, Mg./100 Cc.		Nonultrafiltrable Plasma Calcium, Mg./100 Cc.	
Patient	Sex	Electric Convulsion Treatment Immediately Before	Electric Convulsion Treatment Immediately After	Electric Convulsion Treatment Immediately Before	Electric Convulsion Treatment Immediately After	Electric Convulsion Treatment Immediately Before	Electric Convulsion Treatment Immediately After
M. B.	♀	12.45	14.32	7.92	7.89	4.53	6.43
J. B.	♂	8.16	9.66	3.38	3.40	4.78	6.26
E. L.	♂	8.54	10.68	4.22	4.22	4.32	6.46
J. A.	♂	8.58	9.85	4.00	4.02	4.58	5.83
A. T.	♂	9.92	11.84	4.96	5.15	4.96	6.69
O. S.	♂	11.42	12.96	5.92	5.92	5.50	7.04
O. T.	♀	11.12	12.82	5.13	5.24	5.99	7.58

The values for total, ultrafiltrable and nonultrafiltrable plasma calcium immediately before and after an electrically induced convulsion are represented in table 2. In all 7 patients the total plasma calcium was increased after the convulsion; but, while the nonultrafiltrable calcium showed this increase, the ultrafiltrable calcium did not significantly change on an absolute basis, so that we may say that the increase of plasma calcium following electric shock can be attributed to an increase in the nonultrafiltrable fraction, which consists largely of protein-bound calcium. Nitrogen analyses of the plasma of 2 patients before and after shock indicated, again, that plasma proteins are increased immediately after the convulsion (table 3), and the electrophoretic patterns of the plasma of 1 patient (L. A.) under the same conditions indicated that, within the limits of experimental error, all fractions of protein were increased proportionally.

On the basis of our results and those of other workers who have shown that other plasma constituents increase after shock, hemoconcentration seems to be indicated as one of the phenomena present during an electric convulsion treatment. Consequently, hematocrit determinations were performed on the blood of 5 patients, and in each case the hematocrit value was increased immediately after the convulsion (table 4). Since it was assumed that the change is due to the amount of plasma and that the blood cells remain constant, the circulating plasma volumes were calculated from the hematocrit readings for these patients, and an

TABLE 3.—*Plasma Protein Levels Immediately Before and Immediately After Electric Convulsion Treatment*

Patient	Plasma Protein, Gm./100 Cc.	
	Before Electric Convulsion Treatment	After Electric Convulsion Treatment
A. W.	6.75	8.13
F. P.	8.06	9.09
	(As determined by electrophoresis)	
L. A.	7.80	8.70

TABLE 4.—*Hematocrit Values and Circulating Plasma Volumes Immediately Before and Immediately After Electric Convulsion Treatment*

Patient	Hematocrit Value, Percentage		Percentage Decrease in Circulating Plasma Volume
	Before Electric Convulsion Treatment	After Electric Convulsion Treatment	
S.	43	48	18.8
B.	43	45	8.3
P.	52	55	10.9
Pe.	52	54	7.6
M.	44	46	7.9

average decrease of 10.9 per cent in circulating plasma volume was found (table 4). Our results are in agreement with the recent data of Altschule and associates,[9] who found that hemoconcentration and decreased plasma volume occur regularly after electrically induced convulsions.

Therefore, it seems that hemoconcentration takes place after an electric convulsion treatment, thus accounting for the reported increases in various plasma constituents. However, if this phenomenon were the only factor, one would expect the ultrafiltrable and the nonultrafiltrable plasma calcium to increase proportionally. Our results, however, did not indicate this; the increase was in the nonultrafitrable fraction, whereas

9. Altschule, M. D.; Cram, J. E., and Tillotson, K. J.: Hemoconcentration After Electrically Induced Convulsions in Man, Arch. Neurol. & Psychiat. **59:** 29-38 (Jan.) 1948.

the ultrafiltrable fraction remained essentially the same before and after the convulsion. Some phenomenon, then, other than hemoconcentration must occur during an electric convulsion treatment.

SUMMARY

Plasma calcium levels determined immediately before and immediately after an electrically induced grand mal convulsion showed an increase after the convulsion in each case, the average increase being 15.2 per cent. The initial increase in the total calcium of the plasma immediately after the convulsion was followed by a gradual decrease, which varied with the patient, and the preconvulsion calcium level was reached in all cases within ninety minutes after the convulsion.

The aforementioned increase in total plasma calcium after the convulsion may be attributed to an increase in the nonultrafiltrable calcium fraction (largely protein-bound calcium); the ultrafiltrable calcium fraction remained essentially the same before and after the convulsion.

Plasma protein levels were also increased immediately after an electric convulsion treatment, and the electrophoretic patterns of the plasma of 1 patient under the same conditions indicated that within the limits of experimental error, all fractions of protein were increased proportionally.

Hematocrit determinations on the blood of 5 patients showed an increase in the ratio of red blood cells to plasma in each case. An average decrease of 10.9 per cent in circulating plasma volume was found.

It seems that hemoconcentration occurs after an electrically induced grand mal convulsion, thus accounting for the reported increases in several constituents of the plasma. However, some other mechanism may operate to account for the fact that the plasma calcium fractions do not increase proportionally after the convulsion.

Dr. Henry H. Haines, of the Rochester State Hospital, Rochester, N. Y., assisted in the plasma calcium studies.

University of Rochester School of Medicine, Rochester, N. Y.

Case Report

PERIODIC PARALYSIS ASSOCIATED WITH OBESITY OF HYPOTHALAMIC ORIGIN

Observations in a Case with Changes in the Electrocardiogram and the Serum Potassium Level

CHASKIEL GROSSMAN, M.D.
JERUSALEM

Periodic paralysis, characterized by the unique and impressive muscular paralysis, with loss of reflexes and loss of excitability to electrical stimulation, together with its dramatic onset and transient nature, has always been one of the most peculiar and obscure phenomena confronting the clinician. The disorder known as familial periodic paralysis, and rather vaguely classified in the textbooks as a disease of the voluntary muscles, has been extensively studied since Cavare (1853), Westphal (1885) and Goldflam (1890) [1] made their original observations. Metabolic studies on patients suffering from attacks of periodic paralysis have thrown some light on the changes in electrolytes occurring during the episodes, but the cause and mechanism of this disorder are still obscure.

There is today, nevertheless, increasing evidence that periodic paralysis is a syndrome, rather than a nosologic entity, the paralysis being an external manifestation of a more or less severe and complex paroxysmal neural disturbance, which affects various organs, and not the striated muscles only. One seems justified, therefore, in reporting observations made in a case in which the attack of muscular paralysis was accompanied with unusual neurovegetative features, and the patient had a peculiar disturbance in water metabolism of central origin.

REPORT OF CASE

The patient, an 18 year old girl, had always been in good health until the summer of 1945, when she first noticed fatigue and anorexia. For a few months, the loss of appetite increased, leading frequently to complete refusal of food, and she lost 35 pounds (15.9 Kg.). In September 1945 she was admitted to a hospital in New York for investigation. There, physical examinations, roentgenologic studies and urinalysis revealed nothing abnormal. The temperature was subnormal, the blood sugar was low, the blood cholesterol was increased and basal metabolism was —25 per cent. During the week that she was in the hospital her appetite improved and she gained 9 pounds (4.1 Kg.). She was discharged with the diagnosis of anorexia nervosa. In December 1945 she weighed about 92 pounds (41.7 Kg.). She then suddenly began to gain in weight, and in the course of five days she gained 48 pounds (21.8 Kg.). This was accompanied with a feeling of weakness, and amenorrhea occurred (for the first time since the onset of her menses, at the age of 12, menstruation having previously been normal, of the twenty-eight day type, lasting four days and quite unremarkable). The gain in weight was explained by her family physician as edema due to lack of protein.

From the Department of Neurology, Rothschild Hadassah University Hospital.

1. Goldflam, S.: Ueber eine eigenthümliche Form von periodischer Paralyse, Ztschr. Klin. Med. **19**:1, 1891.

With forced feeding, the patient's weight fell to 125 pounds (56.7 Kg.). In January 1946 there was a second sudden gain, from 125 to 168 pounds (56.7 to 76.2 Kg.) during four days. The school physician could find no edema, though he said that "her tissues were distributed peculiarly." The opinion now was that she had simply become fat, which, to quote the patient, "didn't seem possible to me, as I had eaten very little and I noticed the extra weight suddenly." In July further hospital investigations were carried out. Physical examination was noncontributory. The urine and blood were essentially normal except for consistently elevated cholesterol values of between 341 to 311 mg. per hundred cubic centimeters. The phenolsulfonphthalein test revealed 81 per cent excretion of dye. Determinations of the basal metabolic rate showed values of —23 to —13 per cent, the latter being found after three weeks of treatment with thyroid. Roentgenologic studies and intravenous pyelograms revealed nothing remarkable. The psychiatric opinion was that the patient "was using her organically unsound illness (self starvation) to satisfy latent subconscious desire." She was discharged with her condition unchanged and the diagnosis of anorexia nervosa and was placed in the care of a psychiatrist and her local physician.

In January 1947 the patient came to Palestine. About a week after arriving there, she felt weak, and a severe feeling of thirst arose, accompanied with frequency of micturition, nausea, vomiting and abdominal pain. On February 28, she was admitted to the department with which I am associated as an emergency case with the preliminary diagnosis of coma of unknown origin, possibly drug poisoning. In the ward, examination revealed a rather lean girl, with a pale, masklike face. The head and all the extremities lay motionless. Breathing was stertorous, of the abdominal type, with phases of apnea. There was no reaction to painful stimuli. The eyes were half closed, and the pupils, extremely dilated, showed no reaction to light. The corneal reflexes were absent. There was also loss of the patellar, achilles and abdominal reflexes. There were goose flesh and pronounced pallor. The pulse was regular, with a rate of 75 per minute; the blood pressure was 140 systolic and 60 diastolic, and the abdomen was greatly protruded.

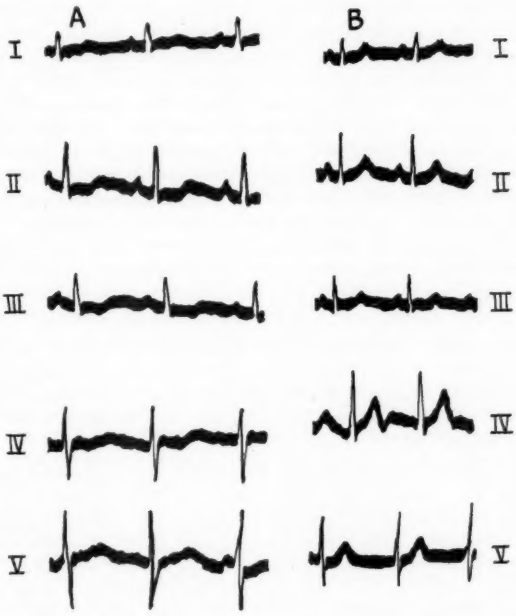
Immediate catheterization of the urinary bladder yielded about 1,500 cc. of colorless urine. Passage of a stomach tube removed about 2 liters of clear fluid; meanwhile, 1 cc. of neostigmine methylsulfate was injected.

The breathing seemed to improve and the impression was gained that the patient was making an attempt to speak, but no words were heard. A faint smile arose on the patient's pale, previously masklike face. The thought that the patient was in full consciousness but totally paralyzed was overwhelming, and the diagnosis of an attack of periodic paralysis was considered. To confirm the diagnosis, an examination of the electrical excitability of nerves and muscles was made. The strongest faradic and galvanic currents did not elicit any contraction, either in the limbs or in the facial muscles. At this time, an electrocardiogram was made, a specimen of blood for determination of electrolytes was taken and 12 Gm. of potassium chlorate was given orally. After thirty minutes the patient began to speak and confirmed the impression that she had been fully conscious throughout and aware of everything happening about her. She said that during the attack she had suffered from agonizing pain, as of "burning like flames," throughout her body. Although she was still unable to move her limbs, there was no impairment of pain, touch and deep sensibility appreciation.

During the following three hours all the voluntary muscles gradually recovered, the first to regain function being those of the face and fingers. The deep reflexes, the abdominal reflexes and normal electrical reaction of the muscles to both the

faradic and the galvanic currents then returned. The pupils slowly recovered their normal size and reaction to light.

The patient stayed five days in the hospital, during which time she felt quite well but showed complete lack of appetite, did not eat but drank a large amount of iced water. She gained 8 pounds (3.6 Kg.) in three days, weighing 112 pounds (50.8 Kg.) on the day of discharge.



Electrocardiograms. *A*, during attack. Pulse rate is 75 per minute; sinus rhythm, regular; P-Q interval, 0.16 second; QRS complex, 0.08 second, and QRST portion, 0.2 second. The QRS complex shows slight slurring. In lead I, the T wave is low and the S-T interval depressed; in lead II, the T wave is positive and low; in lead III, the S-T interval is depressed and the T wave biphasic and low; in lead IV, the T wave is low.

B, after attack. Pulse rate is 90 per minute; P-Q interval, 0.12 second; QRS complex, 0.05 second, and QRST portion, 0.24 second. The T wave is positive and the S-T interval isoelectric in all leads.

Laboratory Data.—The laboratory findings are tabulated as follows, the values being expressed in milligrams per hundred cubic centimeters:

	During Attack	Day After Attack
Serum potassium	8.9	16.0
Serum phosphate	2.5	3.7
Sodium calcium	10.0	10.8
Serum sodium	329.0	178.0
Urea	17.0	18.0
Glucose	153.0	84.0

The urine during and after the attack was normal. The electrocardiogram is shown in the accompanying figure.

Further Clinical Course.—After her discharge from the hospital, the patient "swelled up," from 112 to 138 pounds (50.8 to 62.6 Kg.) in the course of eight days. After five weeks at home, she was again admitted to our department. She had gained 35 pounds (15.9 Kg.), and her body weight at the time of admission was 147 pounds (66.7 Kg.). Physical examination now revealed striking changes in the body outlines. The face was moonlike; the trunk, abdomen and proximal parts of the limbs were "swollen." There was no pitting edema. The whole picture was that of an obese, rather than a swollen, body. The forearms and the calves remained slender. The blood and urine were normal. The volume of excessive extracellular fluid at that time was estimated at 13 liters. Neurologic examination was without pathologic findings. The visual fields were normal. Roentgenographic studies showed a normal sella turcica and mediastinal space, but pronounced osteoporosis of the spine and the pelvis was observed. The electrocardiogram was normal; the blood pressure was 115 systolic and 80 diastolic. Gynecologic examination revealed a hypoplastic uterus but no hirsutism. The temperature was normal; but it is interesting to note that during the patient's stay in the hospital she had two episodes of pronounced elevation of the body temperature, of one day's duration. The first occurred a few hours after a water dilution test, and the second, after psychic excitement.

COMMENT

The episode described was undoubtedly an attack of periodic paralysis. The transitory character of the paralysis, the loss of reflexes and the unique phenomenon of loss of excitability to electrical stimulation of the muscles are classic features of this syndrome. From the clinical point of view, it is desirable to direct attention to the peculiar features of this case.

Contrary to the older view that in the syndrome of periodic paralysis the skeletal muscles are affected selectively, it must be stressed that in this case the participation of the muscle innervated by the sympathetic system was obvious and even dominant. Among other signs, such as pale goose skin, distention of the bladder with retention of urine and accumulation of a great amount of fluid in the stomach without possibility of vomiting, the most prominent was the loss of reaction of the extremely dilated pupils to light. This sign can be interpreted as a result of an extreme stimulation of the sympathetic nervous system. Further evidence in support of this hypothesis is given by findings of hyperglycemia and a raised systolic blood pressure.

It is worth while to stress the interesting behavior of the muscles of sympathetic innervation and those of voluntary innervation, the former showing considerable stimulation and the latter total paralysis. This difference probably gave rise to the impressive finding that, despite total paralysis of all external ocular muscles, the palpebral fissures were half closed only. The action of the nonstriated, sympathetically innervated superior tarsal muscle prevented the total drooping of the eyelids. This sympathetic stimulation produces spasm of the cardia and, by paralysis of the abdominal wall, hindered evacuation of the accumulated fluid in the stomach, through inhibition of vomiting movements. The complexity of all these neurovegetative disturbances points to a mechanism related to a higher autonomic center.

During the attack my colleagues and I found an extreme lowering of the serum potassium level to 8.9 mg. per hundred cubic centimeters and of the phosphate level to 2.5 mg. per hundred cubic centimeters. These changes confirm the findings reported by other authors. The first reports of decrease of serum potassium during

an attack of periodic paralysis were by Biemont and Daniels [2] (1934) and Allott [3] (1935). From this time it has been an almost constant finding, closely related to the syndrome of periodic paralysis. There is also strong evidence of correlation between the level of serum potassium and muscle paralysis, and it was estimated by Aitken, Allott, Castleden and Walker [4] that symptoms of paralysis develop when serum potassium falls below 12 mg. per hundred cubic centimeters. A similar picture of muscular weakness paralleling lowering of serum potassium was seen by Loeb and associates after excessive treatment with desoxycorticosterone in a case of Addison's disease, and by Brown, Currents and Marchand [5] (1944) in a case of paralysis resulting from loss of potassium in chronic nephritis.

Disturbances in the water balance in patient with periodic paralysis were observed by some authors (Kirk and Møller [6]), without being clearly appreciated. In the present case, the negative findings of absence of any organic lesion of the heart or kidneys, a normal plasma protein concentration and absence of pitting edema in a case in which liters of excessive extracellular fluid accumulated during a short time strongly indicated a disturbance of water balance of central origin. Before the attack of paralysis there was a state of polyuria and polydipsia (transient diabetes insipidus). During the attack there was only polyuria, with no water intake, because of paralysis. This caused dehydration. After the attack the patient's body weight soon increased, with the development of a picture of obesity of typical hypothalamic distribution. This may be explained as a result of an exaggerated retention of water during a short period, as there was no excessive food intake. As seen from the history, it was the third episode of such sudden gain in weight. Similar types of obesity were described by Zondek,[7] who stressed the importance of water and salt retention in a great number of obese patients with "water-salt obesity." Together with extreme lability of the vegetative system, disturbed thermoregulation, transient polyuria, menstrual disturbances, osteoporosis and tendency to retention after the water dilution test, this type of obesity is now considered a manifestation of hypothalamic dysfunction.

As seen from the anamnesis and the neurologic examination in our case, there was no history of trauma, encephalitis or clinical signs of a space-occupying lesion, or of syphilitic basal meningitis and vascular softening of the hypothalamus: It is therefore most probable that the condition was a peculiar functional derangement of the hypothalamic region.

Analyzing the above described attack and taking into consideration the recent progress in knowledge of the functions of the hypothalamus, a diffuse hypothalamic "discharge" should be regarded as the underlying cause of the complex neurovegetative and metabolic manifestations observed. As seen from experimental

2. Biemont, A., and Daniels, A.: Familial Periodic Paralysis and Its Transition into Spinal Muscle Atrophy, Brain **57**:91 (June) 1934.

3. Allott, E. N., cited by Walker, M. B.: Potassium Chloride in Myasthenia Gravis, Lancet **2**:47 (July 6) 1935.

4. Aitken, R. S.; Allott, E. N.; Castelden, L. I. M., and Walker, M.: Observations on a Case of Familial Periodic Paralysis, Clin. Sc. **3**:47, 1937-1938.

5. Brown, M. R.; Currents, J. H., and Marchand, J. F.: Muscular Paralysis and Electrocardiographic Abnormalities, J. A. M. A. **124**:545 (Feb. 26) 1944.

6. Kirk, E., and Møller, H.: Studies on a Case of Paroxysmal Myoplegia, Acta. med. Scandinav. **80**:64, 1933.

7. Zondek, H.: Diseases of the Endocrine Glands, ed. 4, Baltimore, Williams & Wilkins Company, 1944; Ueber hypophysär-zerebral-peripherische Fettsucht, Deutsche med. Wchnschr. **51**:1267 (July) 1925.

analogy, a diffuse sympathetic discharge obtained after stimulation of the posterior and lateral hypothalamic nuclei gives the following responses (Fulton,[8] and Kabat, Anson, Magoun and Ranson[9]): (1) dilatation of the pupils; (2) elevation of the blood pressure; (3) piloerection; (4) loss of gastrointestinal peristalsis, loss of tone of the stomach; (5) vasoconstriction, (6) heart acceleration.

All these experimental responses show striking similarity to the clinical features in our case, the behavior of the heart being an exception. There is evidence that during a massive reaction of the hypothalamus, as seen in the case of Penfield,[10] some of the manifestations are attributable to a parasympathetic discharge, but the presence in our case of another important factor, which doubtless had an influence on the whole heart action, cannot be overlooked. This was the low serum potassium level, the profound influence of which on the prolongation of the PQ, QRS and QRST intervals is clearly seen from our electrocardiographic studies. Similar electrocardiographic changes were found by other authors[11] in cases of periodic paralysis and closely resemble those seen in conditions with low serum potassium level from other causes, such as Addison's disease after excessive treatment with desoxycorticosterone, or chronic nephritis, in the case of Brown, Currents and Marchand.[5] It is much more probable, therefore, that an additional factor operates peripherally on the heart muscle, a factor which is to be regarded as a consequence of the lowering of the serum potassium level. The same factor appears to influence the skeletal muscles, with the difference that the latter are much more sensitive and in the same circumstances are more easily deprived of their essential function, contractility. Clinically, therefore, the paralysis shows definite peripheral features, such as loss of mechanical and electrical excitability, this being a manifestation of complete cessation of the function of the muscle fiber. It is the function that suffers, but not the anatomic substratum of the muscle cell, thus making more comprehensible the peculiar phenomenon of the transient nature of the paralysis and the complete recovery after every attack.

The lowering of the serum potassium level is closely related to neurohormonal mechanisms, as seen from the following evidence: Epinephrine lowers the serum potassium level (McArdle and Allott[12]; Castleden[13]). Periodic paralysis can be produced in susceptible persons by administration of large amounts of dextrose, the attacks leading to a pronounced fall of serum potassium. The rise of blood sugar itself is not the causal agent, because attacks can be produced by injections

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8. Fulton, J. F.: Physiology of the Nervous System, New York, Oxford University Press, 1943.

9. Kabat, H.; Anson, B. I.; Magoun, H. W., and Ranson, S. W.: Stimulation of the Hypothalamus, Am. J. Physiol. **112**:214 (May) 1935. Ranson, S. W.; Kabat, H., and Magoun, H. W.: Automatic Responses to Electric Stimulation of Hypothalamus, Arch. Neurol. & Psychiat. **33**:467 (March) 1935.

10. Penfield, W. G.: Diencephalic Autonomic Epilepsy, Arch. Neurol. & Psychiat. **22**:358 (Aug.) 1929.

11. Stewart, H. J.; Smith, J. J., and Milhorat, A. T.: Electrocardiographic and Serum Potassium Changes in Familial Periodic Paralysis, Am. J. M. Sc. **199**:789 (June) 1940. Stoll, B., and Nisnewitz, S.: Electrocardiographic Studies in a Case of Periodic Paralysis, Arch. Int. Med. **67**:755 (April) 1941.

12. McArdle, and Allott, E. N.: Further Observations on Familial Periodic Paralysis, Clin. Sc. **3**:229, 1937-1938.

13. Castleden, L. I. M.: The Effect of Adrenalin of the Serum Potassium Level in Man, Clin. Sc. **3**:241, 1937-1938.

of insulin, which lowers the serum potassium, but of course lowers the blood sugar also (Aitken, Allott, Castleden and Walker [4]).

The close relation of the central neurovegetative manifestations to the severe functional disturbance of peripheral nature appears clearly in the present case. It is a characteristic feature and seems to be significant, as it permits a hypothesis which takes into account the role of the hypothalamus and the metabolic factor, as well, in the pathogenesis of this puzzling syndrome. If, in the light of modern pathophysiologic knowledge, one must stand aloof from such theories as "inhibition of spinal centers" (Cousot [14]), intoxication (Goldflam [1]) and transitory ischemia of the muscles (Schmidt [15]), there remain to be mentioned two apparently different points of view: the "diencephalic" and the "metabolic."

The possibility of the diencephalic origin of periodic paralysis was considered by Mankovsky [16] in a rather intuitive way. He stressed the similarity between cataplectic states and those of periodic paralysis. In both instances there is a sudden relaxation of the muscles with diminution or loss of reflexes and electrical excitability. These considerations and the evidence that the cause of cataplexy is a lesion of the diencephalic region gave the author ground to assume a central pathogenesis for periodic paralysis also. The case reported by Gelbard [17] points in this direction. A woman aged 60 was suddenly stricken with transient flaccid paralysis of the extremities, with all the characteristic features of periodic paralysis. The patient was obese (she weighed 220 pounds [99.8 Kg.]) and had diabetes insipidus and severe somnolence. She died during an attack. Although an autopsy was not performed, the author concluded that the clinical manifestations resulted from a diencephalic lesion, which, according to his statement, gives further evidence of the central origin of periodic paralysis. The other point of view emphasizes the importance of the metabolic changes in the periphery in the pathogenesis of periodic paralysis. Support is lent to this view by the nearly constant finding of lowering of the serum potassium level during attacks. However, as may be observed from the analysis of the present case, and others as well, the metabolic component can in no way be regarded as the cause of the profound disturbances in the neurovegetative system. Indeed, the lowering of the serum potassium seems to be merely a link in the chain of pathologic events, the common origin of which is a central, hypothalamic disturbance. Such disturbances, more or less impressive, may be found in every case of periodic paralysis. The vegetative manifestations are of a more discrete and subjective nature, whereas the muscular paralysis gives the observer a more objective and imposing impression, and in such a way dominates the clinical picture.

If one examines critically the cases reported in the literature, even the first classic descriptions, one at once observes how deeply "imbedded" is the muscle paralysis in the variety of vegetative manifestations, such as prodromal severe thirst and polyuria, complete cessation of peristalsis and urination during the attacks and profuse perspiration, often indicating the end of the attack. It is reasonable to assume that these vegetative manifestations are of central origin and due to a dysfunction of the hypothalamic region. The hypothesis of the central

14. Cousot, G.: Cas de paralysie periodique, Bull. de l'acad. de méd. de Belgique **2**:15, 1886.

15. Schmidt, A. E. K.: Die paroxysmale Lähmung, Berlin, J. Springer, 1919.

16. Mankovsky, B. N.: Ueber die paroxysmale Paralyse, Arch. f. Psychiat. **87**:280, 1929.

17. Gelbard, A.: Paroxysmal Paralysis with Hypothalamo-Hypophysial Syndrome, Neurol. polska **21**:206, 1938.

origin of periodic paralysis is therefore probable in the familial cases too, and should be taken into consideration in the clinical and experimental investigation of the more accessible cases of this group.

SUMMARY

A girl aged 18 had three episodes of sudden gain in weight over a period of two years. Each time, she gained about 40 pounds (18 Kg.) in a few days, acquiring a picture of "acute" obesity, with characteristic hypothalamic distribution. The last episode of a gain in weight was preceded by signs of diabetes insipidus and a severe attack of total paralysis of all voluntary muscles, with loss of reflexes and excitability to electrical stimulation. This was accompanied with a marked overactivity of the whole sympathetic system, loss of reaction of the pupils to light, lowering of serum potassium and electrocardiographic changes. The clinical study of the case supports the view that the condition was due to a peculiar functional derangement of the hypothalamic region. The case supports the hypothesis of a central origin of periodic paralysis.

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Dr. D. Ullmann, of the Internal Medical Division A of the Rothschild-Hadassah-University Hospital, Jerusalem, furnished the electrocardiograms, and Dr. H. Hertz, of the Laboratory of Physiological Chemistry of the Rothschild-Hadassah-University Hospital, made the chemical studies.

News and Comment

THIRD SOUTH-AMERICAN CONGRESS OF NEUROSURGERY

The Third Congress of Neurosurgery was held in Buenos Aires, Argentina, from April 3 to 9, 1949, under the chairmanship of Prof. Ramón Carrillo, executive of the Public Health Department in that country.

At this meeting there were lectures on the previously assigned subjects, "Surgical Treatment of Epilepsy," "Hemostasis in Neurosurgery" and "Lobotomy." Each of these topics was subdivided into chapters, to be discussed by those with widest experience in each country. About 150 papers of the open discussion group were distributed to eleven subcommittees for revision and report.

Besides the representatives of neurosurgery from Argentina, there were official guests from Brazil (Dr. Pimenta), from Chile (Prof. A. Asenjo), from Colombia (Dr. A. Jimenez) and from Peru (Dr. E. D. Rocca). Those specially invited were Drs. Putnam and Poppen, from the United States, and Drs. Busch, Lima, Alcalde, Torkildsen and Olivecrona, from Europe.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Anatomy and Embryology

THE AXIAL ORGANIZATION OF THE NEURAL CREST, STUDIED WITH PARTICULAR REFERENCE TO ITS PIGMENTARY COMPONENT. MAN CHIANG NIU, J. Exper. Zool. **105**:79 (June) 1947.

By dividing the neural fold of Triturus torosus embryos into five segments and isolating each in vitro (Holtfreter's standard solution of sodium chloride or adult celomic fluid medium), the author determined the axial distribution of the pigment-forming cells in the neural crest.

Only a small percentage of cells from the anterior half of the cranial fold differentiate into chromatophores; the bulk of the explant differentiates as brain tissue and epidermis. The results of growth of the posterior half of the cranial fold suggest that cells normally destined to be mesenchyme or cartilage cells may undergo conversion into chromatophores under the influence of celomic fluid. The anterior trunk fold gives rise to mesenchyme cells with a few "giant" cells and a larger percentage of chromatophores than the posterior cranial segment. The posterior trunk fold gives rise to almost exclusive outgrowths of pigment cells. Outgrowths of the caudal fold contain only small percentages of chromatophores (maximum 5 per cent), while most of the cells are mesenchyme cells or myoblasts.

The differences in the number of pigment cells supplied by the various segments were confirmed by grafting these pieces into pigment-free areas on T. torosus hosts.

Extirpation of the trunk folds resulted in a notable reduction or delay in pigment formation on the head and tail; hence, cranial and caudal melanophores must be derived mainly from adjacent parts of the trunk crest.

Complete removal of the cranial folds led to the eventual appearance of a greater than normal number of chromatophores on the head. Even when the trunk folds, the normal source of many head chromatophores, were removed with the cranial folds, the same result was observed. Apparently, potential pigment cells in the head region are held in abeyance by the dominating influence of the intact cranial folds. This control of pigmentary differentiation of cells is revealed when paired pieces of cranial fold are grafted in substitution of short segments of trunk folds. There is a great delay in or prevention of the development of melanophores in the intact region of the body posterior to the grafted folds. This influence of one portion of the crest on another along the body axis may be important to the general problem of neural crest organization.

REID, New Brunswick, N. J.

INSULIN-INDUCED ABNORMALITIES OF BEAK, EXTREMITIES AND EYES IN CHICKENS. WALTER LANDAUER, J. Exper. Zool. **105**:145 (July) 1947.

The injection of insulin into chick embryos at a period later than that considered in previous investigations calls forth abnormalities of the beak, the extremities and the eyes.

In white leghorn embryos the maximum incidence of skeletal defects (beak deformities and micromelia) occurred after injection at the 120 hour stage of

development. Buphthalmos (pronounced bulging of one or both eyes) had its maximum incidence after injection of insulin at the same stage of development. This ocular defect was much less common than the defects of the skeletal system.

In certain stocks, such as creeper fowl, embryos were found to be less susceptible to defects of the beak and extremities in response to injections of insulin at any developmental stage.

Polydactyly (often like one of three genetically distinct types) occurred with low, but significant, frequency among insulin-treated white leghorn embryos. However, in stock of polydactylous fowl, insulin treatment of the embryos tended to shift the result from polydactyly to polyphalangism. In this respect, the effect of insulin resembled that of a well known genetic modifier.

The evidence suggests that certain modifying genes tend to protect embryonic development against interference by detrimental hereditary factors as well as by insulin.

Many of the insulin-produced abnormalities appear to be phenocopies. It is presumed that the developmental steps leading to the gene-controlled abnormalities and their insulin-induced phenocopies have certain biochemical events in common.

REID, New Brunswick, N. J.

REGENERATION AND DEGENERATION EXPERIMENTS ON LATERAL LINE NERVES AND SENSE ORGANS IN ANURANS. MARGARET R. WRIGHT, J. Exper. Zool. **105:** 221 (July) 1947.

The lateral line sense organs of anuran tadpoles (Rana sylvatica, Rana palustris, Rana pipiens) on which hypophysectomy was done at the tail bud stage showed no abnormality of structure, even in an 8 month old tadpole. Normal Rana clamitans tadpoles were also used.

After amputation of the tail tip, lateral line sense organs regenerate from the placodal material of the most posterior organ. These placodal cells differentiate rapidly into typical sense organs, and the full complement of organs to the tail tip regenerates. The regenerating lateral line nerve accompanies the sense organ material after a simple amputation of the tail tip. The process of regeneration is not altered by denervation of the source organ before, after or simultaneously with the amputation. This budding and regeneration of sense organs after denervation casts doubt on the concept of the inductive action of the lateral line nerve.

Denervated lateral line sense organs can maintain their structural integrity for at least one hundred and forty-two days, although some degenerate in less time. The effect of elimination of the trophic action of the nerve on the sense organ is not apparent as soon as has been claimed for some of the fishes. From these results, it seems probable that the normal degeneration of the lateral line organs at metamorphosis is not caused by the mere degeneration of the lateral line nerve trunks.

Regeneration of the lateral line nerve into the former position neither induced the formation of new organs nor caused the reappearance of those which had degenerated. Transposition of the lateral line nerve to a region without the sense organs did not induce the formation of lateral line sense organs at any time during a two hundred day period.

In the anuran lateral line, organs are never formed from ordinary epithelial cells.

REID, New Brunswick, N. J.

Diseases of the Brain

HODGKIN'S DISEASE INVOLVING THE PITUITARY GLAND WITH DIABETES INSIPIDUS. ERNEST I. MELTON and W. L. MCNAMARA, Ann. Int. Med. **25**:525 (Sept.) 1946.

Melton and McNamara report the case of a white man aged 47 with Hodgkin's disease in which "lumps" developed on the left side of the neck. Somewhat later similar masses appeared on the right side of the neck and in the right axilla and groin. There had been considerable loss of weight. For about a month prior to admission the patient experienced progressively increasing weakness and severe thirst. He stated that he drank about 3 gallons (12 liters) of water daily and urinated in almost equal quantity. He noticed no polyphagia.

Lymphadenopathy was present without roentgenographic evidence of mediastinal involvement. The roentgenograms of the skull revealed that the sella turcica and anterior and posterior clinoid processes were normal. The specific gravity of the urine was low, with readings varying from 1.004 to 1.008. The urinary output for twenty-four hours varied from 3,000 to 7,900 cc. A concentration test of the urine revealed poor concentrating power. The blood sugar was 74.1 mg. per hundred cubic centimeters. The glucose tolerance was normal, the urine on all occasions being free from sugar. The patient had bouts of elevated body temperature, with periods in which the temperature was normal. Biopsy of a cervical lymph node established the diagnosis of Hodgkin's disease. The patient received a course of high voltage roentgen therapy. During the course of this treatment intestinal obstruction developed and he died. The pertinent findings at necropsy consisted of evidence of Hodgkin's disease, which involved also the pituitary gland. Melton and McNamara collected from the literature 4 cases of lymphogranuloma involving the pituitary gland. In 1 of these, symptoms of diabetes insipidus were not shown. In the 3 cases in which the syndrome of diabetes insipidus developed various neurologic symptoms, due to involvement of nerve tissue by the lymphogranuloma, also appeared.

GUTTMAN, Philadelphia.

INTRANASAL (SPHENOPHARYNGEAL) ENCEPHALOCELE. FRANK M. ANDERSON, Arch. Otolaryng. **46**:644 (Nov.) 1947.

Congenital herniations of the brain or meninges are considered due to faulty development of the fetal skull, with the protrusion occurring through a cleft between the skull bones or through a bony defect resulting from incomplete ossification. The basal encephalocele is the least commonly observed variety and includes the sphenopharyngeal, spheno-orbital and sphenomaxillary types. In the sphenopharyngeal type the hernial sac is contained within the pharynx or nose, causing obstruction and deformity of the respiratory passages. There is always the danger of cerebrospinal rhinorrhea and meningitis, should the meningeal sac rupture.

Anderson describes the case of a boy aged 11 years who had a sphenopharyngeal encephalocele passing through the cribriform plate of the ethmoid bone and presenting itself in the nasal cavity. At the age of 4 this boy had had a "nasal polyp" removed surgically. The operation was followed by cerebrospinal rhinorrhea and meningitis. After almost seven years he had three more attacks of meningitis within three months. Repair of the encephalocele was then successfully accomplished by the intracranial route.

Although some cures have been reported with use of the external method of repair, the intracranial approach has been found the most satisfactory. Because of its resemblance to a polyp or a nasal fibroma, an encephalocele should be considered in the diagnosis of a spherical mass in the nose or pharynx, especially in infants or children.

RYAN, Philadelphia.

GERIATRICS—EPILEPSY IN OLD AGE. MADELAINE R. BROWN, Geriatrics **2**:231 (July-Aug.) 1947.

According to Brown, epilepsy is thought to be an inherent, inherited abnormality of the nerve cells of the brain, or paroxysmal cerebral dysrhythmia. In the absence of cerebral injury, it would seem unlikely that the onset of cerebral dysrhythmia in the aged would be due to age alone. The case histories of the 2 patients presented here would seem to bear this out. One of the patients was a woman, aged 61, and the other was a man, aged 71 when the seizures started. Each had a sibling who had epilepsy. Neither of the patients had retinal arteriosclerosis, hypertension, glandular dysfunction or Stokes-Adams disease. In both patients recent memory had been poor since the onset of convulsions. There were no abnormal neurologic signs of psychotic behavior. The electroencephalogram of 1 patient was normal and that of the other was abnormal only after hyperventilation. The symptoms of idiopathic epilepsy may begin at any age. The probable cause lies in an inherent dysrhythmia of the cerebral nerve cells.

J. A. M. A.

VALUE OF EARLY RECOGNITION AND EARLY THERAPY IN CEREBRAL PALSY. MARGARET WATKINS, J. Am. M. Women's A. **4**:48 (Feb.) 1949.

According to Watkins, cerebral palsy is widespread, for each year there are born 7 per hundred thousand population. Of these 7, 1 will die in infancy and 2 will be feebleminded, leaving 4 who are treatable or educable. Of these 4, the condition of 1 will be severe, of 2 moderate and of 1 mild. The physician should see that the children with this condition are directed to a center where they can be given the proper therapy, the proper education and instruction. It should be remembered that because of impairment of the neuromuscular system these children do not do automatically those things which they should do, but that they can be taught a different type of muscle control by early training in good patterns of behavior before bad habits are established. The treatment is a combination of physical therapy, occupational therapy and speech therapy. As soon as cerebral palsy is recognized, the baby should be started on conditioned exercises. The parents are taught exercises to be given while a simple rhyme is sung; in other words, conditioned response based on Pavlov's experiments. Through constant repetition of the rhyme and the exercise, passive motion is changed to active assisted motion and, finally, to active motion. The exercises are designed to teach reciprocation of the legs and reach and grasp of the arms and hands.

J. A. M. A.

OPTIC NEURITIS AND SINUSITIS. F. NORTHINGTON and R. L. ROUEN, U. S. Nav. M. Bull. **49**:101 (Jan.-Feb.) 1949.

Northington nnd Rouen present the case of a woman who was hospitalized with a complaint of pain in the left eye, especially on movement of the eye, pain in the region of the maxillary sinuses, and blurring of vision in the left eye. The

present illness began ten days before admission, when she awakened with obstruction to nasal breathing with profuse drainage. The pain and blurring of vision developed on the third day after onset of illness. Examination disclosed a purulent infection of all the nasal accessory sinuses except the frontal sinuses, but the posterior ethmoid and the sphenoid sinuses were chiefly involved. Treatment consisted of administration of penicillin, 30,000 units every three hours; sulfadiazine, 1 Gm. every three hours and thiamine hydrochloride, 25 mg. daily, and irrigations of the sphenoid and maxillary sinuses. The symptoms subsided promptly. On the eleventh day of treatment, the sinuses were clear, visual acuity and visual fields were normal, but the slight elevation of the nerve head persisted and did not subside until about three weeks later. The authors feel that in patients with optic neuritis an examination of the nasal accessory sinuses should be included in the search to determine the cause, and that when a purulent sinusitis is present suitable therapeutic measures should be employed.

J. A. M. A.

ANGIOMA OF THE BASAL GANGLIA. L. J. ROWLEY, Proc. Roy. Soc. Med. **40**:164 (Feb.) 1947.

At the age of 5 years the patient first exhibited a limp; four years later the right hand became weak and weakness of the right side of the face of central type was noted, although the latter had allegedly been present since birth. On examination, at the age of 9 years, a bruit was heard over the left eyeball and the left side of the head; a faint port wine nevus was present above the left eye, and the retinal veins of the left eye showed tortuosity and dilatation. The patient had right hemiparesis, with weakness, wasting and hypotonicity, more pronounced in the arm than in the leg; a Babinski sign on the right; limitation of upward gaze, and convergence. Ventriculographic examination revealed an expanding lesion in the left caudate nucleus, and angiography confirmed the diagnosis of a large angioma in the left basal ganglia.

BERRY, Philadelphia.

Treatment, Neurosurgery

TREATMENT OF SYPHILIS OF THE CENTRAL NERVOUS SYSTEM WITH PENICILLIN. ALBERT HEYMAN, Am. J. M. Sc. **213**:661 (June) 1947.

One hundred and forty-one patients with all types of neurosyphilis were treated with penicillin and the clinical and laboratory results studied. Ten patients received 1,200,000 units of the drug; 63 patients, 2,000,000 to 3,000,000 units, and 63, 4,000,000 units. The author used the changes in the spinal fluid as the primary criterion of the effect of the therapy. In six months 3 of the patients who had received 1,200,000 units had a return of the abnormalities of the spinal fluid, including increase in the cell count and protein content, and a positive Wassermann reaction; 4 of the patients who had been given 2,000,000 to 3,000,000 units had a similar relapse, and 2 who had received 4,000,000 units also had a relapse. The spinal fluid indicated improvement in approximately one-half the patients whose disease was of less than five years' duration, whereas only 6 of the 118 patients with late syphilis obtained a reversal to normal of the spinal fluid. Patients having maximal changes in the spinal fluid including increase in the cell count, protein content and reaction to the quantitative Kolmer test, obtained less satisfactory results after penicillin therapy than did patients with less pronounced changes. No apparent relation was noted between the results obtained in the

spinal fluid and those obtained in the serologic tests of the blood so that in the case of neurorelapse without clinical symptoms only the changes in the spinal fluid were reliable.

Early asymptomatic neurosyphilis and acute syphilitic meningitis responded best to penicillin, but none of the patients with meningovascular syphilis, dementia paralytica, tabes or optic nerve atrophy obtained normal spinal fluids; that is, penicillin was least effective in cases of the more advanced neurosyphilis. There was no relation between the amount of previous treatment and the response to penicillin. Approximately one-half the patients who obtained satisfactory changes in the spinal fluid had had previous adequate chemotherapy. However, the results of fever therapy were somewhat better than those with penicillin for the patients with dementia paralytica.

The clinical response was not striking, as the majority of patients were asymptomatic at the beginning of treatment. There appeared to be subjective improvement, manifested by increased vigor, better appetite and general increase in sense of well-being. Two ataxic patients with tabes had greatly improved gait, and 7 patients with early dementia paralytica obtained improvement in their tremors, handwriting and slurring speech. Only 1 patient showed slight improvement in mental status. An initial febrile Herxheimer effect was commonly encountered. Three patients with dementia paralytica became agitated during therapy, and 1 asymptomatic patient had an acute psychosis. The author concludes that doses of less than 4,000,000 units of penicillin are unsatisfactory in the treatment of neurosyphilis and that the cell count of the spinal fluid is the most sensitive index of the effect of therapy.

MADOW, Philadelphia.

SUPRASCAPULAR NERVE BLOCK IN SHOULDER PAIN IN THERAPY OF SHOULDER PAIN. J. MILOWSKY and E. A. ROVENSTINE, Anesthesiology **10**:76 (Jan.) 1949.

Rovenstine in 1941 introduced with Wertheim the technic of blocking the suprascapular nerve at the lesser scapular notch. The desirability of establishing the block at this point was its accessibility and the fact that no branches from this nerve are given off to the shoulder before it passes through the lesser scapular notch. Suprascapular nerve block was advocated as an adjunct in the treatment of chronic shoulder pain. Milowsky and Rovenstine report on 100 consecutive, unselected patients with shoulder pain; the greatest number was admitted with the diagnosis of bursitis. A good result was obtained in both the acute and the chronic variety in the majority of patients after one block. Three patients with bursitis were not benefited by the suprascapular block. The mode of action of this treatment is not completely understood, but vasodilation may play a part. This would encourage vascularization and facilitate absorption of calcium deposits. Several patients have demonstrated in a follow-up examination roentgenologic evidence of loss of calcium. A second possibility is that relief of pain permits motion, which, in turn, improves vascularization. The effects of suprascapular nerve block on pain of osteoarthritic origin were not uniformly successful. Patients with "idiopathic shoulder pain" experienced alleviation of symptoms after suprascapular nerve block. Supraspinatus and capsular tears may be effectively treated by nerve block if the injury is not complete or massive.

J. A. M. A.

PLASTIC SURGICAL REPAIR OF FACIAL PARALYSIS. PAUL W. GREELEY, Arch. Surg. **56**:132 (Feb.) 1948.

In selected cases of peripheral paralysis of the facial nerve excellent recovery of function is obtained by nerve suture or nerve grafts. The results of spinofacial or hypoglossofacial anastomosis leave much to be desired because of disturbing associated movements. If neurosurgical methods are not feasible, facial paralysis may be corrected by plastic surgery. Support of the paralyzed facial muscles by strips of autogenous fascia give satisfactory results. The use of tantalum wire or mesh is not recommended for this purpose. The method of facial support may be supplemented by transplantation from the temporalis muscle, but, for good functional results, the muscle pedicles must be made large enough to maintain their viability. Furthermore, the muscle-transplanting operation requires systematic retraining of expressive facial movements before a mirror.

C. F. LIST, Grand Rapids, Mich.

THE CONSERVATIVE TREATMENT OF THIRD VENTRICULAR TUMORS. ARTHUR WARD and R. GLENN SPURLING, J. Neurosurg. **5**:124 (March) 1948.

Ward and Spurling report 14 cases of tumor of the third ventricle in which the following course of treatment was used: After a positive diagnosis of a tumor in this region had been made, a subtemporal decompression was performed, followed by intensive irradiation. If, at the end of an adequate period of irradiation, the decompression flap was still elevated and the patient clinically unimproved, direct surgical attack on the tumor was carried out. The occasional colloid cyst could then be removed, and histologic verification of a tumor of malignant type could be made.

Nine of the authors' 14 patients treated in this manner had survived from one and one-half to thirteen years, at the time of the reports. Of this group, 2 had colloid cysts, which were subsequently removed; 1 had a proved malignant glioma, and in the case of the remaining 6 patients there was no need of further surgical intervention after the initial decompression and irradiation.

Five patients had malignant gliomas, proved at subsequent operation, and all died within three years.

The authors believe that if only clinical results are to be thought of patients with tumors of the third ventricle treated in this manner have a lower mortality rate and a shorter stay in the hospital than those treated by a more radical procedure.

TOZER, Philadelphia.

TREATMENT OF SEVERE INTRACRANIAL INFECTION BY REPEATED INTRAVENTRICULAR INJECTION OF PENICILLIN: THEORETICAL AND PRACTICAL CONSIDERATIONS. B. D. WYKE, Surg., Gynec. & Obst. **85**:340 (Sept.) 1947.

Although intraventricular administration of penicillin has been employed sporadically, a systemic account of the theory and practice of this method has not been given. Wyke discusses the factors controlling the passage of penicillin through the blood-brain barrier in the light of previous experience and the results obtained by him in a series of cases. He concludes that therapeutically adequate concentrations of penicillin cannot be maintained for sufficient time in the cerebrospinal fluid by systemic administration of the drug. He considers repeated intraventricular injection of penicillin indicated in cases of purulent intracranial infection with a penicillin-sensitive organism when the cerebrospinal fluid pressure and cell counts

are high; in cases of intracranial infection with highly virulent or partially penicillin-sensitive organisms, especially in children; in cases of intracranial infection with a penicillin-sensitive organism which fails to show early and progressive improvement under medical treatment; in cases of intracranial infection with a penicillin-sensitive organism in which cerebrospinal fluid block is suspected; in cases of intracranial infection in which streptococci are found in the cerebrospinal fluid; in cases in which intracranial operations are to be carried out in the presence of potentially infected foci, and in any case of head injury in which there develops cerebrospinal rhinorrhea, papilledema or coma. The operative technic and the postoperative management of patients given intraventricular injections of penicillin are described.

J. A. M. A.

TREATMENT OF NEUROSYPHILIS WITH PENICILLIN. J. P. MARTIN, Brit. M. J. **1**:922 (May 15) 1948.

Martin reports the results of treatment with penicillin in 24 cases of neurosyphilis at the National Hospital, Queen Square. The series was composed of 8 cases of dementia paralytica, 5 cases of tabes dorsalis, 2 cases of optic nerve atrophy and 9 cases of meningovascular syphilis.

Penicillin, injected intramuscularly, was given at first in courses of 2,000,000 Oxford units, but eventually the dose was standardized at 5,000,000 units. Small doses were administered the first day, but thereafter 60,000 units was given every three hours until 5,000,000 units had been given.

In all but 1 of 18 cases in which clinical progress could be evaluated, progress of symptoms was arrested from the time of the first course of treatment, and in nearly all the patient made recovery. In most instances the Wassermann reaction of the cerebrospinal fluid became negative in about a year. The number of cells in the fluid usually became normal by the end of two months. The total protein content became normal more slowly. The colloidal gold reaction was most resistant to change. Except for the colloidal gold reactions, and occasionally the total protein, the constituents of cerebrospinal fluid returned to normal within a year in all cases in this series. The effects of treatment on the clinical state and on the states of the cerebrospinal fluid and blood all indicated that treatment with penicillin was effective in arresting and exterminating the disease and provided good grounds for expectation that the results would be permanent. Martin concluded from his study that in most cases penicillin alone is usually sufficient in the treatment of neurosyphilis.

ECHOLS, New Orleans.

TEATMENT OF EPILEPTICS WITH EPANUTIN. ROBERT G. R. BURROWS, J. Ment. Sc. **93**:778, 1947.

Burrows treated 196 epileptic patients with sodium diphenylhydantoinate (epanutin®) over a period of six years. The optimum dosage for adults was found to be 1½ grains (0.097 Gm.) three times a day after meals, though at times four or five doses a day were required for control of convulsions. Children above 10 years of age tolerate an adult dose; in younger children it is halved. When the drug fails to bring about satisfactory results, the addition of phenobarbital is often successful. Substitution for other anticonvulsants was accomplished by standard gradual technics. Of the series, 65 per cent showed definite improvement, and 16 per cent had total cessation of attacks. Many apparently deteriorated patients became less apathetic and quarrelsome. Toxic symptoms developed in 30 per cent of the patients.

Transient albuminuria developed in 1 patient, and 6.6 per cent showed hyperplasia of the gums. A few patients went into depressed and confused states, which disappeared on withdrawal of the medication.

BEATON, Tucson, Ariz.

GONOCOCCAL MENINGITIS TREATED WITH PENICILLIN AND SULPHAMEZATHINE. B. P. MOORE, M. J. G. LYNCH, P. C. REYNELL and W. H. DONALD, Lancet **1**:476 (March 27) 1948.

The authors describe the case of a 6 year old girl who became ill with gonococcic meningitis and was treated with penicillin; this case is believed to be the first on record in which this condition was so treated. The patient came to the hospital with acute abdominal pain; appendicitis was suspected and an operation was performed. Purulent free fluid was found in the abdominal cavity, chiefly in the pelvis, with small, flocculent masses of pus and fibrin. The fallopian tubes were edematous. The appendix was removed, and 200,000 units of penicillin was placed in the peritoneal cavity. A course of intramuscular injections of penicillin, 40,000 units every three hours, was begun. Organisms cultured from peritoneal swabs were identified as Neisseria gonorrhœae by colonial appearance and fermentation tests.

Two days after operation the patient complained of frontal headache. Slight nuchal rigidity and a faint Kernig sign were detected. Lumbar puncture was performed, and the same organisms were recovered from the fluid as from the peritoneal swabs. Penicillin was given intrathecally, 40,000 units the first day and 50,000 units the next day. The intramuscular administration of penicillin was continued, the dose being increased to 50,000 units. Three days after onset of symptoms the temperature was still 100.5 F., and sulfamezathine® (the dimethyl derivative of sulfapyridine) was given in addition, 1.5 Gm. at the start and 0.5 Gm. every four hours. Recovery was uneventful thereafter, with no residual symptoms.

MADOW, Philadelphia.

BASOPHILISM TREATED UNSUCCESSFULLY WITH MASSIVE DOSES OF OESTROGENS AND DEEP X-RAY THERAPY, BUT CURED BY RADON SEEDS INSERTED INTO THE SELLA TURCICA. A. C. CROOKE, Proc. Roy. Soc. Med. **40**:153 (Feb.) 1947.

A woman aged 30, eight months post partum, complained of increased weight and broad purple abdominal striae, associated with excess hair on her upper lip, bloated facies and greasy skin, irregularity of menses with subsequent cessation, and cervicodorsal kyphosis. The symptoms began two months post partum. She showed a glucose tolerance curve of diabetic type. Roentgen therapy failed to delay the progression of the symptoms, and 2 radon seeds, each 1.5 millicuries, were implanted in the pituitary gland. Improvement began within nine days. Gradually, during a subsequent period of six years, despite early symptoms of pituitary hypofunction, all symptoms except irregular menstruation subsided.

BERRY, Philadelphia.

DISCUSSION ON THE TREATMENT AND PROGNOSIS OF TRAUMATIC PARAPLEGIA. Proc. Roy. Soc. Med. **40**:219 (March) 1947.

DR. L. GUTTMANN: In the Spinal Injuries Centre at Stoke Mandeville, of 177 casualties, consisting of 108 gunshot wounds and 69 fractures, 119 were lesions of the spinal cord and 58 lesions of the cauda equina. The patients were admitted

at varying periods after injury, many in serious conditions from other wounds or from infection. A total of 13 patients died, 8 within the first year. The two main causes of death from infection and sepsis were bedsores and infection of the urinary tract. Guttmann condemns the use of open suprapubic cystotomy as the method of choice—this method was used in 148 cases, in all of which infection proved serious.

Tidal drainage proved a valuable ancillary method of treatment, especially if used early, except in certain cases of small bladder with uninhibited detrusor action and in some cases of lesions of the cauda equina with rigid bladder walls. Development of automatic reflex activity of the bladder wall in cases of lesions of the spinal cord and voluntary micturition by abdominal pressure in cases of lesions of the lower portion of the cord and the cauda were encouraged. The main factors, whatever the local attack, consisted in shortening the duration of the recumbent position and restoration of the best possible physical fitness of the patient. Various autonomic mechanisms effected profound disturbances in the cardiovascular activity above the site of the lesion. Reflex responses were more conspicuous in cases of complete lesions in the cervical and upper thoracic portions of the cord down to the fifth thoracic level; i. e., the greater part of the splanchnic control was crippled. The stimulus arose from the distended bladder, rectum and colon along extramedullary circuits.

Guttmann emphasizes the importance of physical rehabilitation and stresses the socioeconomic aspects of paraplegia. Physical therapy aims at (1) the prevention of contracture and atrophy and the treatment of spasms and (2) adaptation of the normal parts of the body by compensatory training. Simple occupational therapy is supplemented by the more practical "prevocational training" as soon as practicable. Plaster beds are condemned as contrary to the fundamental principles of rehabilitation of paraplegic patients. The most satisfactory method of control of reflex spasms has been found to be regular passive movements.

Mr. E. W. Riches: The aim of urologic treatment is "to leave the urinary tract free from infection, with a bladder of adequate capacity from which urine can be passed without incontinence, preferably by the natural passage." Drainage is essential but immediate catheterization is harmful, and a delay of twenty-four to forty-eight hours will not seriously impair the function of the bladder or rupture the viscus. The delay will allow time for removal of the patient to a surgical center. In rare instances, because of severe pain, drainage by a serum needle inserted well above the pubis is permissible and may be repeated once if necessary.

For general use, suprapubic catheterization of the distended bladder is recommended, a small 16 French catheter, directed downward and backward under strict asepsis, being used. The catheter is changed after fourteen days and subsequently at weekly intervals. This method is less likely to give rise to renal infection than drainage by the urethral route because of the danger of urethritis and subsequent ascending infection via the lymphatics associated with the latter method, and because ascending infection from the bladder is less likely with adequate drainage. When drainage is effected, it must be continuous, and tidal drainage is the most satisfactory assurance of this. This drainage is maintained while the bladder is paralyzed, until maximum recovery is demonstrated by cystometry, power of emptying and absence of residual urine.

Dr. D. Whitteridge: Studies on the physiologic disturbances produced by distention of the bladder in paraplegic patients revealed that when the lesion was below the level of the fifth thoracic segment vasomotor regulation was still possible, whereas with lesions above this point the area controlled by the vasomotor center

was greatly reduced. With higher lesions distention produced flushing of the face and neck with increased cutaneous temperature and decrease in the temperature of the toes. The blood pressure rose 70 to 160 mm. of mercury systolic and 50 to 90 mm. diastolic. There was an initial drop in pulse rate, with a gradual return toward normal. "There can be no question that our phenomenon is due to a spinal reflex, and it seems likely that distention of some hollow viscera can give rise to a peripheral vasoconstriction, which, in these patients, can spread to involve the whole of the sympathetic vasomotor outflow of the isolated cord."

BERRY, Philadelphia.

CURARE-CONTROLLED ELECTRICAL CONVULSION THERAPY. J. A. HOBSON, J. belge de neurol. et de psychiat. **47**:613 (Oct.) 1947.

The value of convulsion therapy for psychiatric disorders has never been doubted, but certain complications have made the procedure hazardous. Among these complications are compression fractures of the vertebrae. By the use of curare with electric shock therapy, the danger of traumatic complications has been largely eliminated and postconvulsive excitement is reduced. Preliminary curarization allows electric shock therapy to be given patients for whom unmodified convulsive therapy would be dangerous. Mechanical precautions to prevent fractures and dislocations are unnecessary, and since no method of restraint is needed, one operator can carry out the treatment single handed. Care and discrimination are needed, however, when curare is administered as an adjunct to shock therapy.

DEJONG, Ann Arbor, Mich.

SUCCESSFUL TREATMENT OF MYASTHENIA GRAVIS OF THE BULBAR TYPE BY UNILATERAL DENERVATON OF THE CAROTID SINUS. A. THEVENARD, L. LEGER and T. JOURDY, Rev. neurol. **79**:741 (Dec.) 1947.

The authors report in detail their second case of favorable result in the treatment of myasthenia gravis by denervation of the carotid sinus. Their patient first appeared with extrinsic signs of ophthalmoplegia—bilateral ptosis with practically immobile globes in divergent strabismus, facial weakness, nasal voice and myasthenic electrical reaction in numerous muscles. There was no enlargement of the thymus. Prompt and dramatic response was obtained with neostigmine, and this favorable response lasted for approximately four months, when increase of medication no longer brought about improvement. At this point, denervation of the left carotid sinus was followed by improvement, which started about fifteen days after operation and reached a level approximately two months after operation, when reduction in the dose of neostigmine was started. At this time the patient was left with a slight ptosis of the left eyelid. After another eighteen months, improvement again set in, so that the ptosis disappeared; finally, two years after the operation, the patient had discontinued use of neostigmine completely and had maintained improvement up to the time of the report. On detailed testing, three years after operation, no myasthenic electrical reactions were anywhere to be found.

The authors note that in 2 other cases of theirs a similar tendency to improve in plateaus followed this operation, in three stages, and they argue that the late improvement may be a delayed result of the operation. They believe that ideal treatment of myasthenia gravis includes denervation of the carotid sinus on one or both sides after neostigmine has failed to produce a response.

LEGAULT, Washington, D. C.

Book Reviews

Neurobiología delle percezióni (Neurobiology of Perceptions). By Vito Maria Buscaino. Price, 600 lire. Pp. 237. Naples: Esi, Edizioni scient. italiane, 1946.

Buscaino's stimulating book constitutes, as the author states, a contribution to the study of the mechanism of perception, particularly to that of normal and pathologic visual perception. The fundamental purpose of the book is the evaluation of the manner and extent of participation of the neuromuscular peripheral elements, not only in the perceptive processes but also in the processes of representation, memory, illusion and hallucination.

To demonstrate his points, the author illustrates with normal and pathologic cases. One realizes that not only the perception of form but that of orderly movement requires the contribution of peripheral structures. The actual upward and downward motion of the eyeball, with the consequent muscular variations, takes an active part in the setting upright of the retinal image. The author feels that the labyrinth is one of the most powerful systems of formation, deformation and motorization of the visual image. He discusses, therefore, the function of the vestibular system in its relation to the elements of the peripheral ocular musculature and to sensory activities.

Special attention is given to the cortical structure, such as the sensory visual band (Smith) and the interparietal cortical stria (Poetz), as part of the paravisual area. The peripheral muscular structures, considered as a whole, receive a great many stimuli which do not follow the optic pathways; one must therefore admit the existence of a special pathway related to the transmission of such stimuli. The pulvinar and the gyrus angularis are steps in such a pathway. As clinical illustrations, the author cites observations on normal subjects and on patients with various lesions in the optic system.

The processes of representation also require the function of the peripheral ocular muscles, as evidenced by the fact that reevocation of oral images, and even the flow of abstract ideas, is accompanied with variations in the action potential of the ocular muscles, which come into action when one expresses words connected with psychic phenomena. In cases of lesions in the gyrus angularis, it is impossible to judge the spatial position of an object; and in the well known case of Gelb and Goldstein, the patient, wounded in the right occipital lobe, with psychic blindness, was able to read only when he made small writing movements with his fingers.

The function of the retina and of the ocular muscles is examined in the light of most modern physiologic data, such as are furnished by the retinogram. These data are correlated with the activity of a specific anatomic structure which has a central and peripheral function. When such a structure is damaged, there appears a syndrome of sensory aphasia and of optic agnosia, which Buscaino reevaluates in a particular section.

To the calcarine region, Vogt's area 17, belong the elementary components of the objective visual manifestation; to areas 18 and 19, the form and movement of the visual phenomena. These ones are doubly connected with the sensory peripheral structure—by a centripetal and by a centrifugal pathway.

The author describes the visual center and the center of motorization of visual images, with special attention to the sagittal layers of Sachs in the white matter of the occipital lobe and the pulvinar.

From all these data, the necessity of the participation of the peripheral muscular structure of the eyes in the processes of perception, as well as of representation,

memory and hallucination, is clarified. For the first time, the role played by the small peripheral elements, such as the neuromuscular fibers (neuromuscular spindles of Golgi, Ramón y Cajal and Lévi), in the central-peripheral activity of the representation phenomena is predicated.

Finally, the author discusses clearly the arguments of adherents of the associationistic theory, as well as those of the gestalt school, proving that there is practically no disagreement between the two schools. The unity of the latter and the so-called mental chemistry of the former find their origin in the evaluation of the activity of the pathways and of the centers of integration under the influence of neurotropism of functioning neurons (Lugaro).

A study of the stimulating data contained in Buscaino's timely contribution should interest greatly both neurologists and psychiatrists who are biologically minded.

Therapy Through Interview. By Stanley Guy Law. Price, $4.50. Pp. 313. New York: McGraw-Hill Book Company, Inc., 1948.

Drawing on his experiences in twelve prewar years of general practice, Dr. Law, who has since specialized in psychiatry, has written this book "with a desire to aid physicians who find a need for psychotherapy in their practice," by passing on to them the results of his own struggle to attain skill in interviewing. That this is a needed and laudable endeavor no one can deny. That he does not completely succeed is to be expected, for the teaching of psychotherapy, especially technics of interviewing, is a fundamental, and as yet unsolved, problem in psychiatry. That he fails to the degree that he does is due not only to the scientific errors incidental to oversimplification but in great part to his appeasement of what his twelve years in general practice must also have indicated to him, namely, an antipathy of the general practitioner to psychiatry.

This attempt to make the bitter psychiatric pill palatable to the general practitioner accounts for much of the tone and form of this work. It accounts for the consciously modest preface, in which the reader is assured that he "need not fear that the language found here will be beyond his scope . . . [for] if psychiatry could not be written in everyday language this work would never have been completed." It accounts for Dr. Law's repeated intimation that, despite his specialty, he is a general practitioner still. It accounts for the folksy presentation of a typical small town filled with typical small-town people. And, to a considerable degree, it accounts for the liberties he is willing to take with his scientific material.

After three short chapters, in which he discusses the personality of the doctor, compares psychiatry and medicine and superficially evaluates the therapeutic situation, Dr. Law attempts to elucidate interviewing technics by presenting 6 imaginary patients and their imaginary dialogue with him in telescoped interviews. Sticking closely to pat, generally accepted dynamics, and not forgetting his promise to use everyday language, Dr. Law obtains gratifying results in all but 1 case, that of a psychopathic personality. The limitations in this method of teaching psychotherapy are obvious and need not be elaborated here.

Despite the sugar coating, the contrived interviews and the errors incidental to oversimplification, there remain positive reasons for reading this book. One can certainly learn something of what might be termed the amenities of the psychotherapeutic situation. Moreover, Dr. Law expresses an admirable approach to the total personality and his environment. Clearly illuminated is a nonmoralistic, noncensuring, permissive, warm and understanding spirit. If even some of this spirit can be captured, the book will have been worth the reading, though the physician reader will have to look elsewhere if he would understand his patients, and will probably learn those interviewing technics appropriate to his own personality by trial and error.